# THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY, CHENNAI, TAMILNADU


## MADRAS MEDICAL COLLEGE, CHENNAI.

Dissertation on

# "FREQUENCY AND CHARACTERISATION OF DEPRESSION IN SCHIZOPHRENIA"

**Submitted for M.D Degree Examination**

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# CERTIFICATE

This is to certify that the dissertation titled, **"FREQUENCY AND CHARACTERISATION OF DEPRESSION IN SCHIZOPHRENIA"** is the bona fide work of **Dr. MRIDULA PRADEEP**, in part fulfilment of the requirements for M.D. Branch – XVIII [Psychiatry] examination of The Tamilnadu Dr. M. G. R. Medical University, to be held in April 2013. The period of study was from July 2011- October 2011.

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# DECLARATION

I, **Dr. MRIDULA PRADEEP**, solemnly declare that the dissertation titled, **"FREQUENCY AND CHARACTERISATION OF DEPRESSION IN SCHIZOPHRENIA",** is a bona fide work done by me at the Institute of Mental Health, Chennai, during the period from July 2011- October 2011 under the guidance and supervision of Dr. R. JAYAPRAKASH. M.D, D.P.M, Professor of Psychiatry, Madras Medical College.

The dissertation is submitted to The Tamilnadu Dr. M. G. R. Medical University towards part fulfillment for M.D. Branch XVIII [Psychiatry] examination.

Place:
Date:

**Dr. MRIDULA PRADEEP**

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# CONTENTS

# INTRODUCTION

Vertical and horizontal lines spread over a picture forms a grid to permit us close scrutiny of the object in greater detail. The intentions behind classification in any system are also to get help in similar ways. Still there is a possibility that the 'whole' may get blurred when prominence is awarded to 'part'. Attempts to bring clarity in the concepts of mental illness, by sharpening the edges of figure and ground has been and is being more difficult than comparable trials in other branches of medicine. Lots of trimming and pruning by our Psychiatrist ancestors has provided us a beaten path to tread, and even given a chance to look around and comment on the path itself.

Is the beaten path all that clear? Is Schizophrenia so well different from Depression? Some observations made by the senior Psychiatrists made this question more relevant. We are still confused with the issue of making a diagnosis with no help from the laboratory thus far. One psychiatrist makes a diagnosis of depression and the other calls it Schizophrenia. What is worse is that the patient improves with either of the treatments viz. anti-depressants or anti-psychotics. Then what was the problem?

One unpublished study from Karolinska University reported Risperidone with Escitalopram was as good as Clozapine. But Citalopram didn't do the trick. Centrifugal considerations give us some demarcated areas for scanning the relationship between affective disorders and Schizophrenia.

## PRE-PSYCHOTIC, PSYCHOTIC AND POST-PSYCHOTIC

### Pre Psychotic:

The possibility of affective disorders among the close relatives of patients with schizophrenia, turned out to be a significant starting point. There was a possibility of two different disorders in the family tree with probabilities of a combination.

It is common talk among psychiatrists about 'what was apparently Depression turned out to be Schizophrenia, during follow-up. The tendency to brand in an adolescent an 'early Schizophrenia' without any feature of that, and in all probabilities deserving a diagnosis of depression, is not unknown.

### Psychotic Phase:

The points of contact were many. There can be some mood disturbances in Schizophrenia which approximates with Depressive symptoms. The so called negative symptoms have much in common with

depressive symptoms. The medicines used in the treatment of Schizophrenia make the person a ‘zombie’ that he can be mistaken for depression. The cognitive deficits often render the patient withdrawn and lethargic creating a pseudo depressive picture. Many a step inducting the individual to interact with the society may make him acutely conscious of his limitations and sprout an adjustment reaction with depressive features. The person with paranoid disorder runs a greater risk in that a realization that his persecutors are more powerful than him frightens him of the consequences and drives him to consider suicide.

**Post Psychotic Phase:**

Invariably the possibility of realizing what had happened and the knowledge of shameful events that have just receded causing extreme sorrow in those with some insight on recovery is the major consideration. Another thought process is that there was depression in the person during active psychotic process, but shaded from exposure by the umbrella of psychotic symptoms. However it was apparent that the depression was not only in the immediate post psychotic phase but also extended to longer periods. An aggravation of depressive symptoms appeared to predict a relapse too.

Questions keep pouring. If there is Depression in Schizophrenia, - will it alter the strategy of therapy? Would this Depression be the cause

of alarming rate of suicide in Schizophrenia? Is it beneficial to use a dopamine agonist to treat or should we resort to SSRIs? Is psychotherapy holding better promises than pharmacotherapy in these conditions?

With humble intentions to see the light that ought to be at the end of the tunnel this small step is taken.

# REVIEW OF LITERATURE

Though the Kraepelinean dichotomy has remained as a monumental sign post directing the passersby over centuries in practice and research, it has attracted adequate controversies too.

There is no questioning of its authority as a guideline. But the objection comes from the observation that the divisional criteria are more dimensional than categorical. The grouping of variables in varying strengths is found inadequate. We need exclusive criteria that can separate categories that will not let the variable join hands in differing ways to erupt different diagnoses. One such factor is mood incongruent delusion favoring Schizophrenia [Kendler, 1986, Peter McGuffin]

Ian F Blockington is disillusioned with the very concept of Schizophrenia which to him is an ‘improbable entity’. He compares it with religious faith which can accept eco-friendly changes across geographical stretches, for want of concrete concepts [1].

DSM and ICD has promoted with great advantage and remarkable clarity from a pool of confusion, checklist type of diagnostic formulation. It simply permits to combine opposing entities as co-morbidities, which is a gross shift from general principles of Medicine and commonsense diagnosis.

**Is there an association between Depression and Schizophrenia?**

Even the original writings of Emil Kraepelin underline depressive features in Schizophrenia and Psychotic (schizophrenic) features in Depression. Epidemiological studies continue to support the view!

The prevalence rate for depressive syndrome in patients diagnosed to suffer from Schizophrenia has a wide fluctuation in various studies viz, 7% to78% with a modal frequency of 25%. This difference in inferences is attributed to investigator preferences and bias based on defining criteria, methodology employed, cohort status, observed interval etc,. [Siris 2001, Sands 1999, McGlashan 1976, Elk R1986, Van Putten and May 1978,Munro 1984, Leff 1988,Kulhara 1989, Addington and Addington 1990, Lindenmayer 1991, Koreen 1993, Mauri 1995, Markou 1996,Wassink 1999, Muller and Wetzel 1998, Serretti , 2004 ][2]

A life time risk of 81% for depression in patients with Schizophrenia was reported in many studies including The National Co morbidity Study [Kendler 1996, Bland 1987; Hafner 1999; Koreen 1993, Martin 1985]. A point prevalence of Major Depressive symptoms in Patients with Schizophrenia ranged between 10% to 30%.[Baynes 2000; Delahanty 2001; Herbener and Harrow 2002; Messias 2001;Jin 2001; Hafner 1999] . In the Epidemiological Catchment Area Study, patients who fulfilled DSM III criteria for Schizophrenia were found to be 14 to

28.5 times more likely to have a concurrent major depressive disorder than the general population [3]

The attraction of depression to cohabit fair sex in general is known, but not equivocally proved when Schizophrenia is present.

[A Addington 1996; Brunete, 1997; McGlashan and Bardenstein 1990 Messiahs, 2001; Oosthuizen, 2002][4].

The life time prevalence of a major depressive episode in patients with Schizophrenia is around 60%. [5]. In a retrospective study conducted in 203 patients admitted for their index psychotic episode, it was reported that 81% of the patients experienced a depressive episode about four years prior to the current admission.[6,7,8].

The evidences from genetic studies have not accepted the possibility of a pure breed in Schizoaffective disorders. It appears that the two disorders breed independently and may co occur by chance.

Camberwell Register reports life time risk of Schizophrenia as 0.86%; depression of sufficient severity requiring inpatient care as 2.7% and upper limit for chance co-occurance of affective disorders with schizophrenia as 3 in10,000. But we have evidences to show that the association between depression and schizophrenia is not so rare-ruling out the possibility of chance.

Now the question is

**Why is depression shaking hands with Schizophrenia?**

The summation of biological, psychological and environmental risk factors results in the development of depression in schizophrenia. Chronic stress, stigmatization, social isolation, disablement and demoralization are known risk factors for depression.

The devastating nature of Schizophrenia and its social consequences means that most patients with schizophrenia are also exposed to these psychological risk factors for depression [9].

**Stress Vulnerability Model [Stress-Diathesis Model]:**

It is based on the concept that genetic factors make an individual vulnerable to develop a disease and its interaction with the stressors is the mode of operation in disease precipitation. This interaction between genetic load and environmental stress gives a product, the value of which, while crossing the threshold recruits the subject into psychotic population [Zubin 1977].

The vulnerability is in a continuum, the two ends representing the least vulnerable that may never manifest the disorder and the most vulnerable who can never escape the disorder. In between lie the majority with varying weight of vulnerability requiring appropriate stressor to multiply the vulnerability factor to reach the threshold.

The stress factors vary in quality and quantity. They can be biological or psychosocial. Given that background, it is possible to consider that the stress of depression itself can precipitate an episode of Schizophrenia in a vulnerable person with its disturbing influence on hormones, monoamines and sleep. It is all the more provoking to support this hypothesis when one considers that

a) Positive symptoms are seen in combination with depression in schizophrenia more often than negative symptoms, and

b) Treatment of syndromal depression with antidepressants convincingly postpone the relapse of schizophrenic episode.[10,11]

**Depression and Schizophrenia in Family Studies**:

There is a considerable overlap between the genetic predisposition for affective disorder and schizophrenia [12, 13].A family history of mood disorders in patients with Schizophrenia increases their chances of developing depressive symptoms. [15, 16, 17]

Crow T.J has suggested a continuum hypothesis- affective disorders and schizophrenia lying at opposite poles of a continuum of genetic load – the evidences borne by the fact that many relatives of a proband with schizophrenia manifest affective disorder. He suggests the possibility of lesser genetic load representing affective pole and a severe

genetic modification tilting the psychotic pole [18]. This may be compared with Slater's observation [Slater E 1947] that the parents of many of his patients with schizophrenia had depressive features in the absence of psychosis. That the parents who could go on to reproduce had a lighter load of schizophrenic genetic material which could have manifested as phenotype depression of genotype schizophrenia is a plausible explanation.

The researchers have come up with innumerable explanations about the cause of depression in schizophrenia. Some feel that it is the interference produced by neuroleptics on the dopamine reward pathway that is responsible for appearance of the symptoms [19].

**Is Depression in Schizophrenia due to impact of pharmacotherapy?**

The answers 'yes' and 'no' are found, with the negative statement adding value to the existence of depression in Schizophrenia. The concept that a prodromal state presents with symptoms indistinguishable from depression rules out pharmacogenic influence in that presentation [Conrad; Herz and Melville 1980]. The finding that neuroleptic treatment and even Chlorpromazine has helped to improve depressive symptoms in Schizophrenia is significantly amalgamating these depressions with Schizophrenia. [Rifkin A, 1975; Siris SG 1987; Bermanzohn, 1992; Van Putten T 1978]

The concept of ‘Akinetic Depression’ [Van Putten and May 1978] is elusive, in that many authors have found anticholinergic therapy had no more effect than placebo in treating those symptoms [Moller and Zerssen 1981; Johnson 1981].

Depression lifting with antipsychotic therapy gives little chance to consider ‘revealed depression’ which would have remained onstage after antipsychotic therapy. Post psychotic depression has no correlation with neuroleptic medication, and it is recognised as a psychosocial reaction to the awareness of the burden of illness. The term ‘Aphanisis’ introduced by McGlashan refers to residual defects of schizophrenia that may be confused with depression. [20]

**Post Psychotic Depression**:

Roth opined that the patient’s failure in some facet of human relationship results in the psychobiological reaction which manifests itself as post psychotic depression. In other words, he felt that it was the patient’s reaction to the losses he experienced due to the psychotic process.

Whether the depressive symptoms in post psychotic depression have their onset in the post psychotic period or whether these symptoms are unmasked when the psychotic symptoms remit is still under debate.

Reports of positive correlation between the depressive symptoms and the positive symptoms of Schizophrenia and of the good response of the depressive symptoms to antipsychotic medication are in favour of the latter hypothesis [21].

**Reactions to Disappointment and Stress**:

The reactions to disappointment and stress can be either acute or chronic.

Acute reactions leave a traceable track that lead to this reaction from losses, disappointments or bereavement in the recent past. By definition they are short lived.

On the other hand Chronic Demoralisation is a state of severe hopelessness due to real problems that are recurrent or continuous [Frank and Klein]. The culprit in this case is the awareness of the problem. In premorbid high achievers, perceptions of the devastating influence of the psychosis on their life can drive them to desperate levels. Those who realise the limitations and humiliations the psychosis can inlay in every aspect of their life are more prone among the patients with Schizophrenia to develop this syndrome. This is different from the neuro-endocrinal dysregulation of syndromal depression and notably differs from that by the absence of vegetative symptoms. Hence it responds better to

psychosocial remediational approaches than somatic therapies. It is important to recognize this group since they run a high risk of suicide[22].

Yet another group feels that alcohol and other substance abuse patterns which are commonly co morbidities in schizophrenia may be the culprits in the evolution of depressive symptoms in these patients.

A large group argues that depressive symptoms are in fact core features of the schizophrenic phenomenology itself. This thought gains strength from the finding that depressive features are present in the acute stage of the psychosis and often stand side by side with positive symptoms. Further they often remit with anti psychotic therapy.

**Depression as an intrinsic part of the Acute Psychotic Episode:**

Depressive symptoms occurring simultaneously with the psychotic symptoms are viewed by some researchers as a core symptom of schizophrenia. This gave rise to the five dimensional theory of schizophrenia where schizophrenia is postulated to have positive symptoms, negative symptoms, disorganised thought, hostility/ impulsivity and anxiety / depressive symptoms. [Moller 2005][21]

Yet another dimension of thinking is that depressive symptoms may be co-morbidity.

Though there is a large diversity in the arguments put forward, the general weightage over time has been for the stress vulnerability model.

**When does Depression occur in Schizophrenia?**

Before, During and After!

1. Depression as a prodromal feature
2. Depressive symptoms as prominent component of acute episode
3. Post psychotic depression

This last one can be further classified as early post psychotic depression and late post psychotic depression

a. Early post psychotic depression:

This refers to depressive symptoms appearing within 6 months of acute episode of psychosis. Considering the possibility of confusion with residual psychotic symptoms, atypical antipsychotics can be considered as treatment option. An antidepressant can be added if the depressive symptoms are severe and persistent even after treatment with an antipsychotic.

b. Late post psychotic depression:

This appears more than 6 months after the acute episodes. Here an antidepressant like SSRI should be considered as first line of management**.**

In the Indian scenario, SS Raju conducted a study on the co-morbidity of depressive symptoms in patients with schizophrenia. At the time of recruitment, 34 % of patients were found to have depressive symptoms. With 8 weeks of neuroleptics, depressive symptoms abated in 47% of these patients.

These patients were followed up for the next 48 months.

- 10% of patients developed Major Depressive Disorder in the presence of residual symptoms.
- 25% of patients developed depressive symptoms not amounting to a syndrome in the presence of residual symptoms
- 3% developed schizoaffective disorder
- 2% of patients in whom symptoms of schizophrenia had remitted developed major depressive disorder.
- 53% of patients who developed depressive symptoms on follow up had no such symptoms at the onset of schizophrenic illness.[23]

**How does depression manifest in the stage of Schizophrenia?**

The depressive symptoms in Schizophrenia may either qualify for a syndrome in itself or it may be present in subsyndromal proportions.

- **Co morbidity – as a syndrome**
- **Subsyndromal**

Along the longitudinal course of schizophrenia, the depressive symptoms may emerge at various time periods. The significance, effects and treatment of the depressive symptoms vary based on the time period when the depressive symptoms first make their debut. [SIRIS SG 2001]

**Differential Diagnosis**

Depressive symptoms in schizophrenia are usually under reported and under recognised, making the diagnosis of depression in schizophrenia a diagnostic challenge. Various disorders have been recognised which can produce symptoms mimicking depression in schizophrenia. Some important differential diagnosis for depression in schizophrenia is the side effects produced by conventional antipsychotics like akinesia, akathisia and drug induced dysphoria.

The depressive symptoms as such may be due to various reasons as suggested by Bartels and Drake in 1988, [24]

- Depression may develop secondary to organic factors.
- Depression may be intrinsic to the acute psychotic episode.
- Depression which is separated from the psychotic episode temporally, like depression in prodrome, post psychotic depression etc.

**Depressive symptoms that are secondary to Medical and Organic factors:**

Various medical and organic factors can produce symptoms of Depression in a patient with Schizophrenia. This includes pulmonary infections, neurological, cardiological, metabolic or endocrine disorders, anaemia, cancer and autoimmune diseases. Certain drugs used in treatment such as beta blockers, non-steroidal anti-inflammatory drugs, indomethacin, sulphonamides, anti-neoplastics, sedative hypnotics and barbiturates can cause depressive symptoms. Discontinuation of cortico-steroids or psycho stimulants can also produce similar symptomatology. Abusing substances like alcohol, cocaine, cannabis or narcotic substances can also cause depressive features. Abstaining from regular supply of legal substances like caffeine and tobacco, often on medical restrictions

as in many in-patient units may pose an added reason to mimic depression [24]

**Neuroleptic Induced Dysphoria:**

Dopamine blockade in the meso-limbic pathways by conventional neuroleptics can lead to anhedonia and depression. If Schizophrenia is conceived as the state of Dopamine dysregulation, the positive symptoms may reflect the storms of dopamine and the negative symptoms the droughts. Then it will be reasonable to see that slight excess of neuroleptics in therapy can bring down the affect to get a label – neuroleptic induced depression. Drug induced dysphoria has been one of the causes behind poor compliance in patients with Schizophrenia. However, the results from most studies remain controversial till date. [Buckley, 2009; Hausmann A, 2002; Siris SG 2003, DJ King, 1995]. Many depressive features remit along with psychotic symptoms during the treatment with neuroleptics.

**Akinesia:**

Akinesia is induced by antipsychotic medications and it can present in a blatant or subtle form. In the blatant form, the patients present with a Parkinsonian gait, stooped posture and diminished arm swing. This is due to the involvement of large muscle groups.

The subtle form of akinesia is easily confused with depression. It involves the small muscle groups. Involvement of facial muscles produces a lack of facial responsiveness which is confused with a low mood. It also impairs the patient's ability to initiate and sustain motor activities [25]. This may be mistaken for the psychomotor retardation of depression. Patients with akinesia are prone to dysphoria [Rifkin A , 1975]. It was Van Putten who introduced the term "akinetic depression" to describe a patient with akinesia, blunted or depressed affect and apathy [Van Putten 1978]. The addition of anti-Parkinsonian medication results in a dramatic improvement in these patients,[Van Putten 1987,Siris SG ]. While the effect is not so evident in depressive symptoms, there are indeed studies which have pointed to positive results in patients with depression when treated with Trihexyphenidyl.

Many anti-parkinson drugs like Levodopa, Seligiline and Pramiprexole are known to have antidepressant properties though to a lesser degree.

**Akathisia:**

This is another movement disorder that can be triggered by moderate dose of high potency antipsychotic medications [Van Putten, 1985]. This also has a blatant and a subtle variety. In the blatant variety the patient often paces and has difficulty remaining seated. The subtle

form is not so dramatic and the patients may merely talk excessively or wander. This presents a picture simulating the psychomotor excitement or agitation which may be a part of depression. Akathisia also has a dysphoric component in which the patient appears agitated or restless and may be mistaken to have agitated depression. Akathisia produces an inner sense of restlessness which when paired with a profound dysphoria, may culminate in suicides and homicides. [Shear k, 1983; Schulte JR, 1985; Drake RE, 1985]

**Negative Symptoms of Schizophrenia:**

Many features of negative symptoms of schizophrenia are identical to depressive phenomenology. The lack of initiative, social withdrawal, anhedonia, reduced speech and activity can be easily mistaken for depression. Differentiating between negative symptoms and depression often poses a diagnostic challenge. However the salient features of depression such as depressed mood, pessimism, guilt and suicidal thoughts help to differentiate it from the negative symptoms of schizophrenia.

**Schizoaffective Disorder:**

The term schizoaffective psychosis was first coined by Kasanin. He used this term to describe a psychotic disorder with an amalgam of

affective and schizophrenic symptoms. Patients with schizoaffective depression are difficult to distinguish from the patients exhibiting depressive symptoms in schizophrenia. However in schizoaffective depression, the depressive symptoms must fulfill the criteria for a major depressive disorder. Genetic studies do not support the view that schizo affective disorder can be a pure breed. McGuffin P et al 1982 report on three sets of triplets. They had a mixture of Manic Depressive Psychosis or Schizophrenia in pure form and only one had indication of schizoaffective disorder. Twin studies of probands suffering from schizoaffective disorder too did not support the possibility of schizoaffective disorder as a heritable pure form. Studies vary with relatives in some having affective disorders more often and others picking schizophrenia with preference. In one study of Schizophrenia and Manic DepressivePsychosis marriages there was no intermediate form. Probably it is always a chance occurrence and not a true breed [26,27].

**Prodrome of Psychotic Relapse:**

Depressive symptoms frequently precede relapse. [Donlon and Blacker; Docherty]. The symptoms of dysphoria, agitation, anxiety, inability to concentrate, social withdrawal, lack of appetite and lack of sleep were noticed to occur quite frequently in the early stages of psychotic decompensation. These usually last for few days before they

are over taken by the psychotic upheaval. The onset of the symptoms is sudden and more like an Agitated Depression in contrast to Depressive syndrome. Family members will be able to identify the symptoms easily and hence psycho- education can help to initiate treatment early and nip the psychotic symptoms.

**Post Psychotic Depression**:

This diagnosis is reserved for depressive episodes occurring in the aftermath of a psychotic illness. This has been regarded as the natural consequence of recovery from an acute psychotic episode, at which time the patient becomes aware of the events of the psychosis and develops a reactive depression.

**Reactions to disappointment and stress**:

As discussed earlier, the reactions to disappointment and stress can be either acute or chronic.

Acute reactions leave a traceable track that lead to this reaction from losses, disappointments or bereavement in the recent past. They are fairly short lived.

Chronic Demoralisation , as discussed earlier is a state of severe hopelessness in premorbid high achievers due to perceptions of the devastating influence of the psychosis on their life [22].

**Depression that is intrinsic to the Acute Psychotic Episode:**

Among the various considerations the most parsimonious view of why depression is so prevalent among patients with Schizophrenia is that like the positive symptoms and negative symptoms which are part and parcel of Schizophrenia, depressive symptoms are also a part of the natural course of Schizophrenia [28].

What are the implications?

**Impact of Depression on Schizophrenia:**

**Prognosis:**

Bleuler viewed depressive symptoms in schizophrenia as a positive prognostic indicator. Few researchers like Semrad equated the appearance of depressive symptoms to the development of a higher level of psychological defence mechanism which opened new avenues for psychotherapy [Semrad EV 1966].Many clinicians since then believed that the appearance of depressive symptoms in schizophrenia signals the process of recovery [Langfeldt G,1937,Roth S,1970]. However the literature in this aspect is somewhat divided. Few investigators have found depressive symptoms to be predictive of a better outcome [Kay SR 1987,Vaillant GE 1964] but some have found them to be negative prognostic indicators [McGlashan ,1976; Mandel Mr ,1982].

Depression in chronic schizophrenia seems to be an unfavourable sign and it has been found to be associated with a greater risk of relapse [Johnson DAW,1988; Mandel MR 1982, Herz MI 1980,1985 ; Himmelhoch 1981] and suicide [Siris SG,1991,2001; Drake RE ,1986; Caldwell CB,1990; Cohen LJ ,1990; Roy A 1982; Black BW 1985]. Depressive symptoms have been found to be associated with impairment in everyday functions [Glazer W 1981; Serban G 1979 ; Cohe C 2000],poorer quality of life, increased rates of hospitalisation [Johnson DAW 1981 ; Falloon I , 1978] and suicides.

This division in literature may be due to various reasons, including the differences in defining depression, different patient population [acute versus chronic] and different levels of psychosis.

**Predicting Relapse:**

Statistically significant correlation was found between the severity of depressive symptoms and the frequency of relapse in schizophrenia [Johnson DA 1988] [29]. Ander Heiden W reported in his study that the correlations between the amount of depressive symptoms during a psychotic episode and the frequency of relapses were found to be statistically significant. [30]

**Suicide:**

Schizophrenia has an augmented risk of both depression and suicide. It has been estimated that 10% of patients with Schizophrenia commit suicide [57]. People suffering from schizophrenia who exhibit suicidal behaviour, both attempts and completions, are found to have significantly more depressive symptoms. Perhaps the most frequently identified risk factor for suicide in Schizophrenia is the appearance of depressive symptoms. [Beisser and Blanchette 1961; Niskanen 1974; Achte 1966; Sletten 1972] The greater parts of patients with Schizophrenia who commit suicide have experienced depression before the attempt. [Cohen, 1964; Roy 1982]

Risk of suicide is particularly high in depressed patients with Schizophrenia in the first few months after diagnosis and after discharge from the hospital. Hopelessness as a symptom is a strong contributor to suicidal behaviour in patients with Schizophrenia. [Virkunnen 1976; Drake 1986] According to Beck, hopelessness has been shown to co-relate with suicidal intent, and subsequent suicide.

There is a high level of subjective distress reported by patients suffering from schizophrenia, who attempt suicide [Cohen,]. The subjective distress experienced by these patients may go unrecognized by

their clinicians perhaps ascribed to psychosis or neuroleptic treatment rather than a distinguishable affective syndrome per se.

Specific treatment of affective symptoms in Schizophrenia helps in suicide prevention [31].

Suicide victims among patients with schizophrenia were achievers premorbidly, and they had high aspirations against a backdrop of painful awareness of their illness. [Drake 1984].

Among the various subtypes of Schizophrenia, patients with the paranoid subtype were found to be more likely to attempt suicide as they tend to be more rigid about their original expectations and usually perceive their difficult prospects for the future much more clearly. These patients have an inherent inclination to project their fears and feelings of despair on the world in general. These patients may be obdurate about possible options for the future and tend to look at suicide as the only option to end their anguish. [Jerry F.Westermeyer and Martin Harrow]

**Social Functioning:**

Social functioning is grossly impaired in patients with schizophrenia. The appearance of depressive symptoms in Schizophrenia further impairs the social functioning. Studies have documented that depressed mood surpassed all other symptoms in schizophrenia in

contributing to the decline in social function. [Glazer, 1981; Serban,1979]. Participating in social leisure activities and the performance of social roles were particularly affected [32]. Greater degree of insight has been found to be a contributing factor for the poor quality of life in these subjects [33].

A strong association has been found between change in functional outcomes and change in depression status in long term treatments of patients with schizophrenia. Hence paying special consideration in treating the depressive symptoms in patients with schizophrenia can go a long way in recovering their overall functioning [34].

Siris , reported that the longitudinal studies exploring the course of schizophrenia have found depressive symptoms to be rampant during all stages of schizophrenia. Evidence suggests that depressive symptoms are associated with impairment in everyday functions, poor quality of life and greater need for medications and hospitalization. Siris, has reported that depressive symptoms increase mortality rates in these patients by contributing to their high rate of suicide.

**Impaired Memory:**

The appearance of depressive symptoms in schizophrenia has been found to have a negative impact on the person's memory functions. [Burt

DB, 1995]. The encoding process in the organisation of memory becomes deficient in these patients. [Weingaartner H 1986]. The degree of memory impairment has been found to be positively correlated with the severity of depressive symptomatology. [Smith MJ, 1994][35]. Evidences suggest that the decreased left prefrontal lobe function in schizophrenic patients may be responsible for the appearance of depressive symptoms and memory impairments in schizophrenia. [Fletcher PC 1995, Dolan RJ 1993]. Treatment with anti psychotics has not produced significant improvement in memory and it has been proposed that the addition of an antidepressant might be beneficial.

## Which factors overlap and smudge the picture?

### Negative symptoms and Positive symptoms

Though phenomenologically the depressive symptoms seem to mimic the negative symptoms, studies are not in favour of a positive correlation between these two variables. On the contrary, positive symptoms have been demonstrated to have a positive correlation with depressive symptoms appearing in these patients [Zisso ,1999;Norman and Malla , ,1991;Sax KW ,1996 ; Barnes , 1989 ; McKenna PJ,1989; Prosser ES, 1987; Hirsch SR,1989][36,37].

In a study by Kulhara, it was seen that the characteristic symptoms of depression other than retardation, slowness and lack of energy had poor to negative correlation with negative symptoms [38]. Tharyan and Kuruvilla studied the correlates of depressive symptoms in patients with schizophrenia and found that retained insight and lower negative symptom scores were more common accompaniments of a mild depressive state developing in these patients [39].

Individually, various psychotic symptoms have been linked with a raised risk of emergent depression. Studies of the phenomenology of depression have discovered that between 66%- 75% of persons with auditory hallucinations will exhibit at least moderate depressive symptoms due to the experience [Chadwick, Brichwood 1994, 1997; Trower, 2004]. The presumed threat from persecutors is enough to generate depressive symptoms, particularly if the person feels vulnerable and exposed. Studies by Norman and Malla and Hirsch, emphasise that there is a positive correlation between depressive symptoms and positive symptoms of schizophrenia [40]

Norman and Malla have suggested that in the relationship between depressive symptoms and the positive symptoms of Schizophrenia the most robust feature is the association between depressive symptoms and reality distortion. The left medial temporal

lobe, the origin of reality distortion with its close link to the limbic system explains the coupling.

Baynes, in their study found that persistent depressive symptoms are related to the degree of persistent positive symptoms and the patient's perception of the extent of social support [58]

**Extra pyramidal symptoms:**

Though there is an apparent phenomenological overlap between the depressive symptoms and extrapyramidal symptoms, no positive correlations have been documented.

**Insight:**

Tharyan and Kuruvilla found that retained insight is one of the factors associated with the development of depressive features in schizophrenia. It has also been shown that during acute schizophrenia, the insight will not be lost completely [ Brichwood , 2000] and this available insight may be adequate to trigger a depressive reaction if the patient's appraisal of the illness is associated with 'shame', 'loss', and 'entrapment'. Tania, found that insight was related with increased suicidal ideation or actions. Increase in insight was found to cause increase in depressive symptoms.

Apart from this, studies have shown that the treatment of patients with schizophrenia with insight -focused CBT and non-CBT approaches targeting insight increased the incidence of depression in these patients[41, 42].

**Atypical antipsychotic:**

There are various reasons why the presentation of depression in schizophrenia treated with atypical antipsychotic is different from Schizophrenia treated with conventional neuroleptics, although this needs to be confirmed by careful investigations. The incidence of akathesia, akinesia, and drug induced dysphoria and negative symptoms which are very close differential diagnosis of depression in Schizophrenia are much less in patients treated with atypical antipsychotics. [Tandon R , 1997; Marder , 1994; Jones H , 1997; Meltzer HY , 1989;Tollefson , 1997; Beasley , 1996] The quality of life measures have also been found to be superior in patients on atypical antipsychotics and hence reactions to stress may be reduced.[Tollefson GD , 1999,Franz M , ,1997] Various studies have reported that atypical antipsychotics have direct antidepressant effect [Azorin ,1995,Tran ,1997; Tollefson ,1999,Beasley 1996, Keck , 1998; Emsley , ,2003]. In addition clozapine has been found to have antisuicidal properties.[Walker ,1998; Meltzer ,1995 ]

**What are the specific tools for assessment?**

The Calgary Depression Scale for Schizophrenia [CDSS] was developed by Addington, specifically for assessing the depressive symptoms occurring in patients with Schizophrenia [43]

Collins demonstrated that this scale is methodologically superior when compared to other scales like HAM D and Becks Depression Inventory. [44]

**What are the implications in treatment when Depression is with Schizophrenia?**

The first step in the treatment of depression in schizophrenia is considering the possible differential diagnosis.

The second step is to exclude organicity.

In the event of recent onset depressive reaction, the various possibilities which have to be considered after excluding organicity are an acute stress reaction or the prodrome of a psychotic episode.

If the patient is at high risk of suicide, he may require hospitalisation. In all other cases, the most appropriate initial response is to increase surveillance, provide additional support and reassess the patient after a week.

An acute stress reaction will resolve spontaneously, and an incipient psychotic episode will soon manifest itself. In the latter case, the psychotic episode can be promptly treated with appropriate antipsychotic agent.

If at the follow –up visit, patient's depressive symptoms persist but psychotic symptoms have not progressed, evaluate for possible extra-pyramidal features which may be subtle and difficult to rule out. If the patient is restless and there are features of akathisia, a trial of benzodiazepine can be given.

If the patient is hypoactive, consider a trial of an anticholinergic anti-Parkinsonian agent, such as Benztropine, for akinesia.

After ruling out extra-pyramidal symptoms, the next possibility to be considered is antipsychotic – induced dysphoria. In this case the neuroleptic dose can be decreased after making sure that there are no active psychotic symptoms.

The other option is substituting the conventional neuroleptic with an atypical antipsychotic. Various studies have shown that the atypical antipsychotics have antidepressant property. Marder, in 1997 did two double blind studies which showed that Risperidone produced greater reduction in depressive symptoms when compared to haloperidol [45]

Olanzepine was found to be superior to haloperidol in bringing down MADRS scores in a prospective study conducted by Tran, and Tollefson [46]. Similarly Quetiapine was also found to be more effective than conventional neuroleptics in treating depressive symptoms in Schizophrenia [Emsley, 2003] [47]. Treatment in neuroleptic resistant patients with Schizophrenia with Clozapine has evidenced a drop in the suicide attempt rates from 25% to 3.5 %[ Meltzer and Okayli] [48] Walker, also reported a significant decrease in suicidality with Clozapine.

In circumstances where the episode of Depression persists in a patient who is already on treatment with atypical antipsychotic, the existing literature does not give much guidance regarding the further management. Among the atypical antipsychotics, Risperidone is known to have mild Parkinsonian effect .Hence if the patient is on Risperidone, the dosage can be tapered or an anti-Parkinsonian drug can be added. Substituting an atypical antipsychotic for another is the other possibility. Care should be taken to see to it that anticholinergic drugs are not combined with Clozapine because it may produce severe autonomic side effects.

If the depression still persists, consider adding an adjuvant antidepressant medication. Both tricyclic antidepressants [49] and Selective Serotonin Reuptake Inhibitors [50] have been found to be effective as

adjunctive antidepressants [Hogarty GE, 1995; Siris SG 1994; Singh AN 1979 ] . With tricyclic antidepressants, the central and peripheral anticholinergic effects like urinary retention, constipation, delirium and cognitive dysfunction may be particularly troublesome. The antiadrenergic effect of these drugs produce postural hypotension and their antihistaminic effects produce sedation. SSRIs are relatively safe even in overdose situations [51] and hence safe with potentially suicidal patients.

Based on their study, Koreen et al, opine that in patients with acute schizophrenia, most of the depressive symptoms remit with the antipsychotic treatment and that the addition of an antidepressant might retard the antipsychotic response to the neuroleptic drug. They feel that antidepressants should be limited to patients who continue to have depressive symptoms even after the psychosis has remitted. [52]

Prescribing antidepressants concurrently with antipsychotic medication is a common clinical practice [11% to 43%]. At times the antidepressants have been found to aggravate the psychotic symptoms [Prusoff 1979]. In a study conducted by Maria Ladea in 2010, it was reported that Escitalopram and Venlafaxine proved to be safe when used along with antipsychotic medications in patients with schizophrenia.

In few reports, lithium has been reported to have a favourable outcome. Lithium augmentation would be helpful for dealing with suicidal ideation. The positive outcome has been particularly seen in patients who had previous affective episodes, a family history of affective disorder or an overall episodic nature to the clinical course. However more research is needed since the evidence supporting the use of lithium in these patients is generally lacking.

Determining the temporal appearance, duration, quality and severity of depressive symptoms is necessary for diagnosis and formulation of an appropriate treatment plan. It was estimated that 38% of all subjects entering the CATIE for treatment of schizophrenia were being treated with a concomitant antidepressant. There is evidence to support the use of these drugs in this co morbid state, although most randomized trials in this area are neither large nor of the highest quality. [Psychol med 2003]

Though it is true that there are evidences supporting the use of adjuvant antidepressants, researchers feel that their use should be limited to cases where an optimal dose of neuroleptic and a trial of atypical antipsychotic have been inefficient [53].

Even with pharmacotherapy, some symptoms tend to remain. Psychosocial therapies have been shown to be effective in alleviating these residual symptoms and improving the social functioning and quality of life. Hence attempts to augment the treatment with a combination of various psychotherapeutic modes are called integrated psychological therapy. [K.Felmet,][54].

The various components of the psychosocial therapies include psycho education, social skills training, assertive community treatment, family intervention, cognitive remediation and cognitive behavioural therapy. It is observed that each component of psychotherapy has specific domains e.g: understanding symptoms and nature of the disorder; social skills training to enhance social interaction and facilitate job opportunities; Family therapy to correct expressed emotions, therapy adherence and prevention of relapse; cognitive remediation to improve neurocognitive functioning. Integrated Psychological Therapy [IPT] has been found to be beneficial in patients with depressive symptoms in schizophrenia. Change, even in a positive direction can be stressful and hence patients with Schizophrenia benefit from nonspecific support and psychosocial rehabilitation services[55] .Though gender differences have not been reported as a factor influencing treatment response, one study

reported the females to benefit more from pharmacotherapy [Hogarty , 1995; Massimo C , 2008].[56]

An ‘International survey of Depression in Schizophrenia’ was carried out by D. D. Addington, to evaluate the clinical approaches in this area. Though majority of respondents acknowledged the considerable clinical burden of depressive symptomatology in Schizophrenia, there was however, little agreement on the best management strategy. [59]

# AIMS & OBJECTIVES

With this background the current investigation aims at observing,

1. The frequency of depressive symptoms at a point in time in patients with Schizophrenia.

2. To analyze the pattern of depressive phenomenology in relation to the different stages of the illness and schizophrenic symptomatology.

3. To understand the depressive symptoms on the background of Deficit syndrome and drug induced EPS.

4. To observe the relationship of depressive features with insight and functioning.

# HYPOTHESIS

1. There is a positive correlation between CDSS/HAMD scores and scores on positive symptoms scale of PANSS.

2. There is no positive correlation between CDSS/HAMD scores and scores on negative symptoms scale of PANSS.

3. Significant number of patients with Schizophrenia have symptoms of Depression when compared to standardized general population statistics.

4. There is a significant positive correlation between CDSS/HAMD scores and age in patients over 50 years of age.

5. There are no correlations between scores on CDSS/HAM D and scores on EPRS.

6. Patients on atypical antipsychotic for more than a month have low scores on CDSS scores than patients who have been on typical antipsychotic.

7. There is a significant positive correlation between higher scores on Schedule for Assessment of Insight [SAI] and CDSS scores.

8. Prevalence of Depressive symptoms in Schizophrenia is higher in patients who have a positive family history of mood disorder or suicide or alcohol dependence.

9. There is a positive correlation between scores on GAF and CDSS scores.

# MATERIALS AND METHODS

The study was carried out at **The Institute of Mental Health, Chennai**.

**Sample Size** – 80 subjects

**Sampling Method** – Consecutive patients coming to the Out Patient Department who fulfilled the inclusion criteria were included in the study.

**Study Design** - Cross-Sectional study

**Inclusion Criteria:**

1. DSM IV TR criteria for schizophrenia at the time of assessment.
2. Age between 18 to 60 years.
3. Both genders.
4. Patients with all the subtypes of schizophrenia who are cooperative for interview and assessment.
5. Patient and relative giving consent.

**Exclusion Criteria:**

1. Any axis-I disorders other than schizophrenia.
2. Co-morbidities like Diabetes, Hypothyroidism, and Dementia.
3. Patients on Anti-depressants.
4. Mental retardation as per DSM IV TR.

**Instruments:**

A semi-structured proforma was administered for all the subjects after getting an informed consent. The proforma contains the demographic profile of the patient, family history and illness characteristics.

All the subjects were administered the following instruments at the time of recruiting the subjects for this study.

1. Positive And Negative Symptom Scale
2. Calgary Depression Scale for Schizophrenia
3. Hamilton Depression Rating Scale
4. Extra pyramidal Symptom Rating Scale
5. Schedule for Assessment of Insight
6. Global Assessment of Functioning Scale

**1. PANSS:**

This scale was developed by S.R. Key, This 30 item scale was specifically developed to assess individuals with Schizophrenia. It consists of a semi-structured clinical interview.

This scale has thirty items. A seven point continuum is used to rate the 30 items. This scale was devised following extensive research and it has included essential elements from other important scales. Eighteen items from the Brief Psychiatric Rating Scale [BPRS] [Overall and

Gorham 1962] and 12 items from the Psychopathology Rating Scale [PRS] have been included as a part of this scale [Singh and Kay 1975a]. Alpha-Co-efficient analysis has indicated high internal reliability among PANSS items with co-efficient ranging from 0.73 to 0.83[P<001] for each of the scales. The split half reliability of the general psychopathology scale was demonstrated to be 0.80[P<001].

The final score of PANSS is arrived at by summation of ratings across items so that the potential ranges are 7- 49 for the positive and negative scales and 16 to 122 for the General Psychopathology Scale. The composite Scale is calculated by subtracting the negative from positive score, this yields a bipolar index that ranges from -42 to +42.

**2. Calgary Depression Scale for Schizophrenia [CDSS]:**

This scale is developed by Donald Addington. The Calgary Depression Scale for Schizophrenia [CDSS] is a nine item scale which was developed specifically to assess Depressive symptoms in schizophrenia. It has been extensively evaluated and appears sensitive to change. The differentiation of depression from negative symptom and extra-pyramidal side-effects of neuroleptic medication is a challenge. Previous studies have shown that it is reliable and valid, particularly in assessing depression regardless of negative symptoms and extra pyramidal side-effects. In contrast to the Hamilton Depression Scale, it

has fewer items and considerably less overlap with the positive and negative symptoms of Schizophrenia. Items do not focus on weight change and initial insomnia, both of which can be confounded by the drug treatment of Schizophrenia.

Score above 6 points on the CDSS has been proposed to separate schizophrenia patients with depression from those without depression; a further study has found optimal cut-off Values of at least 7 points as related to major depression and CDSS scores of at least 4 points to detect minor depression in schizophrenia patients. However, studies directly comparing the accuracy of the CDSS and the HDRS for separating clinically graded mild, moderate, and severe depression in schizophrenia is still lacking.

All items are rated on a four-point scale:

0=absent

1=mild

2=moderate

3=severe.

The first eight items are rated on the basis of the patient's responses to questions; the ninth item is based on the clinician's assessment of the patient over the course of the interview.

The Calgary Depression Scale for Schizophrenia serves as the most appropriate instrument for a dimensional assessment of depressive

symptoms in Schizophrenia. However the earlier scales like HAM-D are also being used in various studies.

**Receiver Operator Curve for Prediction of Major Depressive Episode:**

| CDSS Score | Specificity% | Sensitivity% |
|---|---|---|
| 5 | 74 | 100 |
| 6 | 77 | 92 |
| 7 | 82 | 85 |
| 8 | 91 | 85 |
| 9 | 94 | 69 |
| 10 | 97 | 69 |
| 11 | 98 | 62 |
| 12 | 99 | 54 |
| 13 | 100 | 54 |

[Addington D, *Br J Psychiatry [Suppl 22]* 1993; 163 [Suppl 22]

**3. HAM-D:**

This scale was developed by A Hamilton. This scale has been widely used to measure the symptoms of depression. HAM-D is an observer rating scale consisting of 17-21 items.

Ratings are made on the basis of the clinical interview and other available information .This scale is very effective in detecting the somatic symptoms of depression.

Many versions of the HAMD have been made, but probably the most popular is based on 17 variables. Some variables are graded on a scale of 0-4and others on a scale of 0-2.

The HAM-D version with 17-items, has a mean reliability of [0.81], the 21-item version exhibits a mean reliability only slightly higher than the previous one [0.83]. Therefore, the HAM-D version that mostly recommended is that of 17 items, because adding four items produces negligible reliability improvement.

The HAM-D scores are interpreted as

| | |
|---|---|
| 0-7 | none or minimal depression |
| 8-17 | mild depression |
| 18-25 | moderate depression |
| 26+ | Severe depression |

**4. Extra pyramidal Symptoms Rating Scale:**

The Extra pyramidal Symptom Rating Scale was developed to assess four types of drug induced movement disorder; Parkinsonism, akathesia, dystonia and tardive dyskinesia .Studies found higher inter

rater reliability correlations in both antipsychotic induced movement disorders and idiopathic Parkinson disease.

The Extra pyramidal Symptom Rating Scale specificity was investigated and it was found that Extra pyramidal Symptom Rating Scale measurement of drug induced extra pyramidal symptoms is valid and discriminative from psychiatric symptoms. Inter-rater reliability significance was demonstrated at the 0.01 level.

**5. Schedule for Assessment of Insight [SAI]:**

The SAI developed by A David is a three item rating scale used to evaluate insight in psychotic illness.

This scale evaluates insight in 3 dimensions.

1. The recognition of mental illness
2. The ability to recognize abnormal mental events as pathological
3. Treatment compliance.

Responses are scored on a 0-2 scale.

Responses are scored on 0-2 scale [0=never, 2==often]

It has been reported to have a correlation 0.527 with the BPRS total and 0.525 with the Beck total. Total score is14. Higher score indicates better insight.

**7. Global Assessment of Functioning:**

The Global Assessment of Functioning is a modified version of the Global assessment Scale [GAS], first appeared in DSM-IIIR in 1914.

Overall function on axis V of the DSM-VI is assessed using the Global Assessment of Functioning scale.

This scale may be particularly useful when the clinical progress of a patient needs to be assessed in global terms using a single measure. The Global Assessment of Functioning scale is rated with respect to psychological and occupational functioning only.

The reliability ranges from 0.62 to 0.82

These scales are administered at the time of intake of the subjects. The Psychotic symptom pattern and severity is measured by PANSS. The depressive symptoms are measured by HAM-D. This scale is widely used to measure the depressive symptoms in non-psychotic patients. Hence the Calgary Depression Scale for Schizophrenia [CDSS] is being used to assess the depressive symptoms in psychotic patients.

# RESULTS

**SUMMARY OF RESULTS**

## 1. Socio-demographic and clinical details:

The study group was a homogenous sample consisting of 80 patients.

The demographic details were as depicted in **Table-1 and Table-2.**

The mean age of the study sample was 31.80[SD 8.519].The mean educational standard in years was 7.46[SD 5.024].

Out of the 80 patients 57.5 percent were males and the remaining 42.5 percent were females.50 percent of them were unmarried,43.8 percent were married and only 6.3 percent were separated and living alone.

82 percent of the study population belonged to Hindu religion, 15 percent were Christians and 2.5 percent were Muslims.

Half [50%] of the study group were dwelling in urban setting and 50% were living in rural settings.

55% of the study group were earning below 900 rupees per month,3.8% were earning 900 to 3000 per month.30% of them were earning 3001 to 9999 per month and a meager group were getting more than 10,000 rupees per month.

## 2. Details of Illness variables:

The detailed description of the illness variables including the type of Schizophrenia, number of episodes, duration of illness and number of hospitalization were depicted in **Table-3 and Table-4**.

The mean age of onset was 25.20[SD 5.024] and mean age at first hospitalization was 28.5[SD 7.780]

The mean duration of untreated psychosis was 25.51[SD38.662].The mean duration of the illness was 8.09[SD3.123] months.

Table-4 describes the details of the percentage of illness parameters.

52.5 percent of the study group was suffering from undifferentiated Schizophrenia and 46.3 percent belonged to Paranoid Schizophrenia subtype. Only 1.3 % was diagnosed to have a catatonic sub type of Schizophrenia.

90% of the population had only one episode of illness during their natural course of the illness and 10% had more than one episode.

## 3. Familial inheritance:

The family history of Psychiatric illness, alcohol dependence and suicide were demonstrated in **Table-5**.

A positive family history of mood disorder or Schizophrenia independently were found in 10% of study design. It is worth observing that out of eight probands who had family history of schizophrenia, seven had features of depression and out of eight who had a family history of schizophrenia, none had features of depression. There was a positive family history of suicide in 5% of first degree relatives, 3.8% of second degree relatives and 1.3% of third degree relatives.

12.6% had a positive family history of alcohol dependence syndrome [10%, first degree relatives, 13%, second degree relatives and 13%, third degree relatives]. However these were not statistically significant.

**4. Psychopathology of the study group :[ Table-6[a]**

**Positive symptoms, Negative symptoms and General Psychopathology;**

The mean total PANSS score of the study population is 52.24[normal baseline value-=30].

The mean score on sub scales were,

PS [sum of Positive symptom Score] = 15.249 [SD 3.033] [Range=7-49]

NS [sum of Negative symptom score] = 11.49 [SD 3.819] [Range=7-49]

GP [General Psychopathology Score] = 25.61[SD 4.777] [Range 16-112]

The cut off score for severe cases were 210.The average score for stable out-patients was 60-80.The score for In-patients was 80-150.

The study group falls under the category of "**mild category"** in terms of psychopathology.

The composite index [CI] is -9 to+18[normal range—42-42] indicating predominantly positive symptoms.

**4. Depressive symptoms in Schizophrenia:[Table-6[b]]**

This population had a mean Calgary depression rating scale score of 4.46[SD6.737].

A score above 6 on CDSS is proposed to separate depression in schizophrenic population from Schizophrenia without Depression. One study has found optimal cut-off value of at least 7 as "**Major Depression** "in schizophrenic subjects and at least 4 to detect "**Minor Depression**"

Hence the current study group qualifies for "**Minor Depression**" category.

The mean score on the HAM-D [Hamilton Depression Rating Scale] measurement was 9.41. [Range=0-7].

A score of 8-13 on HAM-D indicates "**mild**" in severity of depression. Both the specific Calgary Depression Scale for Schizophrenia score as

well as the severity in HAM-Dscale clearly depicts that the current study group has mild depression associated with schizophrenic psychopathology.

**5. Extra pyramidal symptoms associated with schizophrenic symptomatology:**

**[Table-6[c]]**

The mean score on extra pyramidal symptoms rating scale was below one in all the four subscales demonstrating that the study populations did not have significant extra-pyramidal symptoms during the assessment.

**6. Functional outcome in Depression with Schizophrenia:**

**Table [6b]**

The mean value on Global Assessment of Functioning Scale [GAF] was 5.90[SD.922].

A GAF score of >5 indicating moderate function and the degree of functioning goes up above 5.

The current study group belongs to "**moderate functioning**" persons with Schizophrenia.

7. **Insight in depression with Schizophrenia: Table [6b]**

The mean score value on Schedule for Assessment of Insight was 2.04[2.378].

The maximum total score representing the three dimensions of insight is 24. Considering the maximal score on insight which indicates better insight, the study group having mean value of 2.04 indicates "**poor insight**.

8. **Correlation between demographic factors and illness characteristics:[ Table 11]**

The age of the subjects correlated positively with the age of onset and the duration of untreated psychosis [$p<0.05$].

Education in number of years had a significant negative correlation with age of onset of the illness [$p<0.01$] and HAM-D score [$p<0.01$].

Duration of untreated Psychosis had a positive relationship with negative symptoms score of PANSS and Global assessment of functioning [GAF] score at 0.05 level of significance.

## 9. Correlation between Psychopathology dimensions of Schizophrenia and Depression in Schizophrenia:[Table 12]

The General Psychopathology score [GP] of PANSS had a positive correlation with Negative Symptom [NS] [$p<0.05$] and negative correlation with positive symptoms [PS] [$p<0.01$].

The General psychopathology [GP] score correlated positively with CDSS score and HAM-D score [$p<0.05$]

## 10. Correlation between functional outcome, Insight and Depression in Schizophrenia: [Table 13]

The CDSS score and HAMD Score had a significant positive correlation with SAI [Schedule for assessment of Insight] score [$p<0.05$]

HAMD Score had a negative correlations with GAF [Global assessment of functioning score [$p<0.05$].

## LIST OF TABLES:

### Table-1: Socio-demographic details of the study design

| **Variable** | N[**cases**] | **mean** | **SD** | **Range** |
|---|---|---|---|---|
| Age | 80 | 31.80 | 8.519 | 18-58 |
| Education | 80 | 7.46 | 5.024 | 0-16 |

### Table-2: Socio-demographic details in percentage

| ***Variable[n=80]*** | ***Frequency*** | ***percentage*** |
|---|---|---|
| **GENDER** | | |
| **Male** | 46 | 57.5 |
| **Female** | 34 | 42.5 |
| ***MARITAL STATUS*** | | |
| ***Unmarried*** | *40* | *50* |
| ***Married*** | *35* | *43.8* |
| ***Separated*** | *5* | *6.3* |
| **Religion** | | |
| **Hindu** | 62 | 82.5 |
| **Christian** | 12 | 15 |
| **Muslim** | 2 | 2.5 |

| | | |
|---|---|---|
| **Occupation** | | |
| **Manual** | 43 | 53.8 |
| **Unskilled** | 6 | 7.5 |
| **Skilled** | 17 | 21.3 |
| **Residence** | | |
| **Urban** | 40 | 50 |
| **Rural** | 40 | 50 |
| **Income** | | |
| **<900** | 44 | 55 |
| **900-3000** | 3 | 3.8 |
| **3001-9999** | 24 | 30 |
| **>10,000** | 9 | 11.3 |

**Table-3: Description of Illness variables**

| *Variable* | *N=[80]* | *mean* | *SD* | *range* |
|---|---|---|---|---|
| ***Onset age*** | 80 | 25.20 | 5.024 | 13-48 |
| ***DUP*** | 80 | 25.51 | 38.662 | 1-216 |
| ***Age of FH*** | 80 | 28.51 | 7.780 | 3-54 |
| ***DI[months]*** | 80 | 8.09 | 3.123 | 0-19 |

**DUP**-Duration of Untreated Psychosis

**Age of FH**-Age of First Hospitalization

**Table-4: Frequency of illness variables.**

| *Variable* | *Frequency* | *Percentage* |
|---|---|---|
| ***Paranoid schiz*** | 37 | 46.3 |
| ***Undiff. schiz*** | 42 | 52.5 |
| ***Catat schiz*** | 1 | 1.3 |
| ***Ist episode*** | 72 | 90 |
| ***>1episode*** | 8 | 10 |

**Schiz**==Schizophrenia

**Undiff**==Undifferentiated

**Catat**==Catatonic

**Table-5: Family history [frequency table].**

| *Variable* | *Frequency* | *%* |
|---|---|---|
| **Mood disorder** | 8 | 10 |
| **Schizophrenia** | 8 | 10 |
| **Suicide** | | |
| **1st relative** | 8 | 10 |
| **2nd relative** | 1 | 1.25 |
| **3rd relative** | 1 | 1.25 |
| **Alcohol** | | |
| **1st relative** | 8 | 10 |
| **2nd relative** | 1 | 1.25 |
| **3rd relative** | 1 | 1.25 |

**Table-6[a]: mean scores of the measurements.**

| Scale | N=[80] | mean | SD | Normal Range |
|---|---|---|---|---|
| **PANSS PS sum** | 80 | 15.24 | 3.003 | 7-49 |
| **PANSS NS sum** | 80 | 11.49 | 3.819 | 7-49 |
| **CI score** | 80 | 3.75 | 5.430 | -42-+42 |
| **GP score** | 80 | 25.61 | 4.777 | 16-112 |

**PS**-Positive syndrome [P1-P7]

**NS**-Negative Syndrome [N1-N7]

**CI**-composite Index [P-N]

**GP**-General Psychopathology

**PANSS total Score=52**.24[Normal Baseline Score=30]

**Table-6[b]: mean values of Depression Rating,**

**GAF and Schedule of Assessment of insight.**

| Scale | N | Mean | SD |
|---|---|---|---|
| CDSS score | 80 | 4.46 | 6.737 |
| HAM-D score | 80 | 9.41 | 7.833 |
| GAF score | 80 | 5.90 | 0.922 |
| SAI score | 80 | 2.04 | 2.378 |

**CDSS-Calgary Depression Scale for Schizophrenia**

**HAM-D-Hamilton Depression Rating Scale**

**GAF-Global Assessment of Functioning**

**SAI-Schedule for Assessment of Insight**

**Table-6[c]: mean values of ESRS scale.**

| Scale | N | mean | SD |
|---|---|---|---|
| **ESRS-1** | **80** | **0.10** | **0.409** |
| **ESRS-2** | **80** | **0.10** | **0.439** |
| **ESRS-3** | **80** | **0.00** | **0.000** |
| **ESRS-4** | **80** | **0.00** | **0.000** |

**ESRS scale- ExtraPyramidal Symptom Rating Scale**

**ESRS-1—Parkinsonism, dystonia and Dyskinesia: Questionnaire**

**ESRS-2—Parkinsonism**

**ESRS-3—Dystonia**

**ESRS-4—Dyskinetic Movements**

**Table.7**

## Test Statistics

| | Mann-Whitney U | Wilcoxon W | Z | Asymp. Sig. (2-tailed) |
|---|---|---|---|---|
| Age | 766.000 | 1942.000 | -.020 | .984 |
| Education | 674.500 | 1850.500 | -.927 | .354 |
| onset age | 557.500 | 1085.500 | -2.072 | **.038** |
| Dur untre | 710.500 | 1238.500 | -.571 | .568 |
| 1st hospi | 734.500 | 1262.500 | -.330 | .741 |
| DOI | 574.000 | 1750.000 | -1.911 | .056 |
| PS | 731.500 | 1259.500 | -.361 | .718 |
| NS | 685.500 | 1861.500 | -.814 | .415 |
| CI | 726.500 | 1254.500 | -.409 | .683 |
| GP | 636.000 | 1812.000 | -1.301 | .193 |
| Anergia | 742.000 | 1270.000 | -.287 | .774 |
| Thot dist | 654.500 | 1830.500 | -1.136 | .256 |
| Activa | 754.500 | 1282.500 | -.139 | .889 |
| Paranoid | 662.000 | 1838.000 | -1.057 | .290 |
| Depressi | 679.000 | 1855.000 | -.979 | .327 |
| CAL tot | 671.000 | 1847.000 | -1.086 | .278 |
| HAM tot | 740.000 | 1916.000 | -.276 | .783 |
| GAF | 700.500 | 1876.500 | -.704 | .482 |
| SAI tot | 642.500 | 1818.500 | -1.265 | .206 |

**Table.8**

**Chi-Square Tests (family history of schizophrenia)**

| | **Value** | **df** | **Asymp. Sig. (2-sided)** | **Exact Sig. (2-sided)** | **Exact Sig. (1-sided)** |
|---|---|---|---|---|---|
| Pearson Chi-Square | 1.353(b) | 1 | .245 | | |
| Continuity Correction(a) | .869 | 1 | .351 | | |
| Likelihood Ratio | 1.361 | 1 | .243 | | |
| Fisher's Exact Test | | | | .260 | .176 |
| Linear-by-Linear Association | 1.336 | 1 | .248 | | |
| N of Valid Cases | 79 | | | | |

a. Computed only for a 2x2 table

b. 0 cells (.0%) have expected count less than 5. The minimum expected count is 14.52.

**Table.9**

**Chi-Square Tests (family history of suicide)**

| | **Value** | **df** | **Asymp. Sig. (2-sided)** | **Exact Sig. (2-sided)** | **Exact Sig. (1-sided)** |
|---|---|---|---|---|---|
| Pearson Chi-Square | .036(b) | 1 | .850 | | |
| Continuity Correction(a) | .000 | 1 | 1.000 | | |
| Likelihood Ratio | .036 | 1 | .850 | | |
| Fisher's Exact Test | | | | 1.000 | .570 |
| Linear-by-Linear Association | .035 | 1 | .851 | | |
| N of Valid Cases | 79 | | | | |

a Computed only for a 2x2 table

b 2 cells (50.0%) have expected count less than 5. The minimum expected count is 3.75.

**Table.10**

**Chi-Square Tests(family history of mood disorder)**

| | Value | df | Asymp. Sig. (2-sided) | Exact Sig. (2-sided) | Exact Sig. (1-sided) |
|---|---|---|---|---|---|
| Pearson Chi-Square | 4.215(b) | 1 | **.040** | | |
| Continuity Correction(a) | 2.820 | 1 | .093 | | |
| Likelihood Ratio | 4.759 | 1 | .029 | | |
| Fisher's Exact Test | | | | .061 | .043 |
| Linear-by-Linear Association | 4.161 | 1 | .041 | | |
| N of Valid Cases | 79 | | | | |

a Computed only for a 2x2 table

b 2 cells (50.0%) have expected count less than 5. The minimum expected count is 3.75.

**Table-11:**

**Pearson's/Spearman's[r] correlation co-efficient of demographic variables with disease variables [n=80]**

| | *Age at onset* | *DUP* | *HAMD score* |
|---|---|---|---|
| ***Age*** | **.727**** | **.270*** | |
| ***Education*** | **-.409**** | | **-.236*** |
| ***PANSS [NS]*** | | **.267*** | |
| ***GAF*** | | **.270*** | |

***correlation is significant at the 0.01 level**

****correlation is significant at the 0.05 level**

**Table-12:**

**Pearsons/Spearman's[r] correlation co-efficient of depression scores with mean scores on PANSS [n=80]**

| | *CDSS score* | *HAMD score* | *PANSS [GP]* |
|---|---|---|---|
| ***PANSS [PS]*** | | | **-.222*** |
| ***PANSS [NS]*** | | | **.333**** |
| ***PANSS [GP]*** | **.627**** | **.570**** | |

***correlation is significant at the 0.01 level**

****correlation is significant at the 0.05 level**

**Table-13:**

**Pearsons/Spearman's[r] correlation co-efficient of mean scores on CDSS and HAM-D**

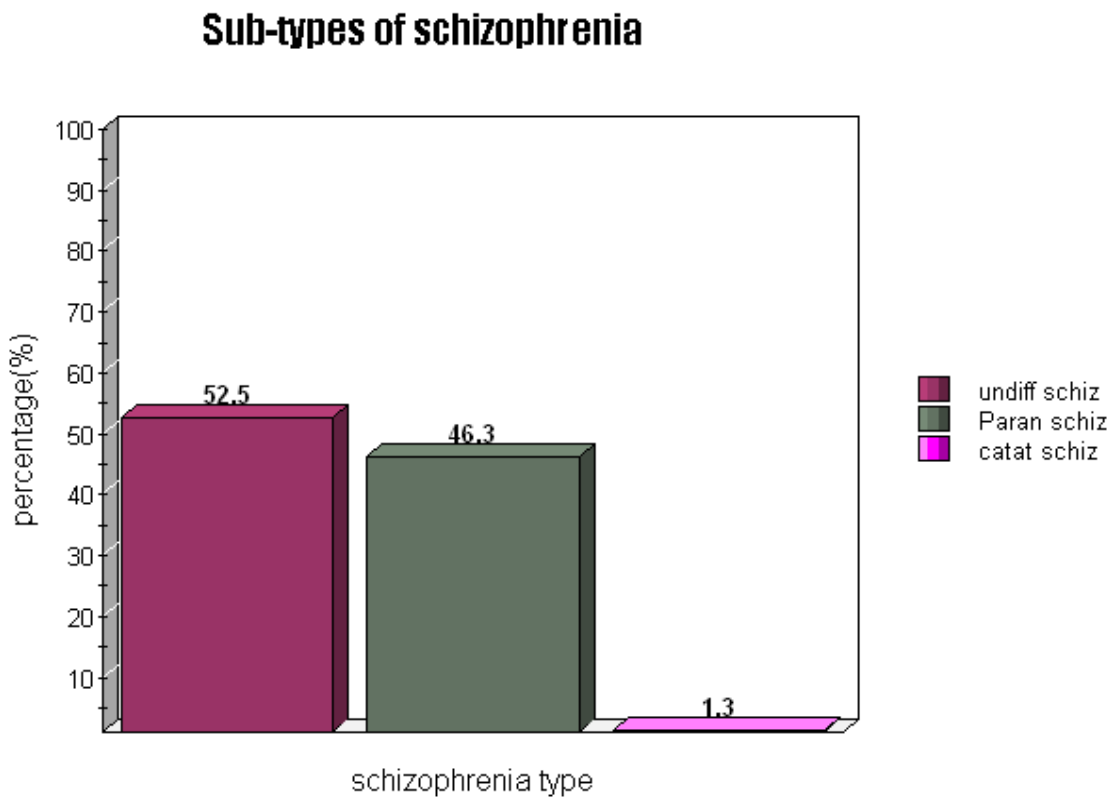
| | ***PANSS[GP]*** | ***SAI score*** | ***HAM-D*** |
|---|---|---|---|
| ***PANSS [GP]*** | | | **.570**** |
| ***CDSS score*** | **.627**** | **.464**** | **.866**** |
| ***HAM-D score*** | | **.392**** | |
| ***GAF*** | | | **-.287**** |

***correlation is significant at the 0.01 level**

****correlation is significant at the 0.05 level**

## LIST of Diagrams and Graphs

## Diagram 1



# Diagram 2

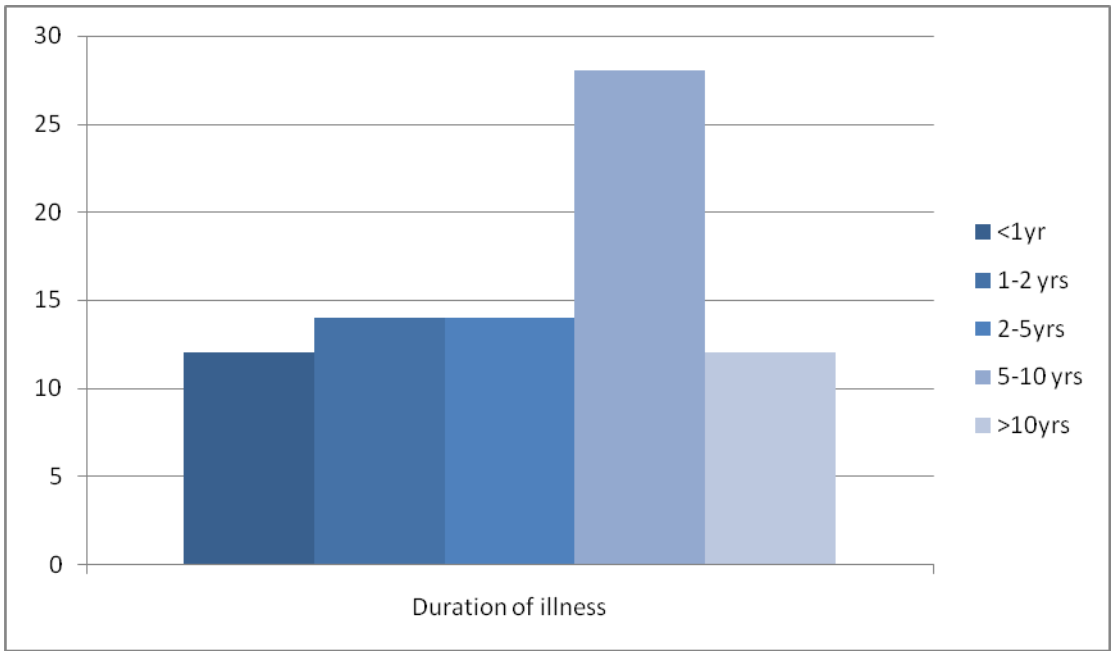

30
25
20
15
10
5
0
Duration of illness
<1yr
1-2 yrs
2-5yrs
5-10 yrs
>10yrs

**Diagram 3**

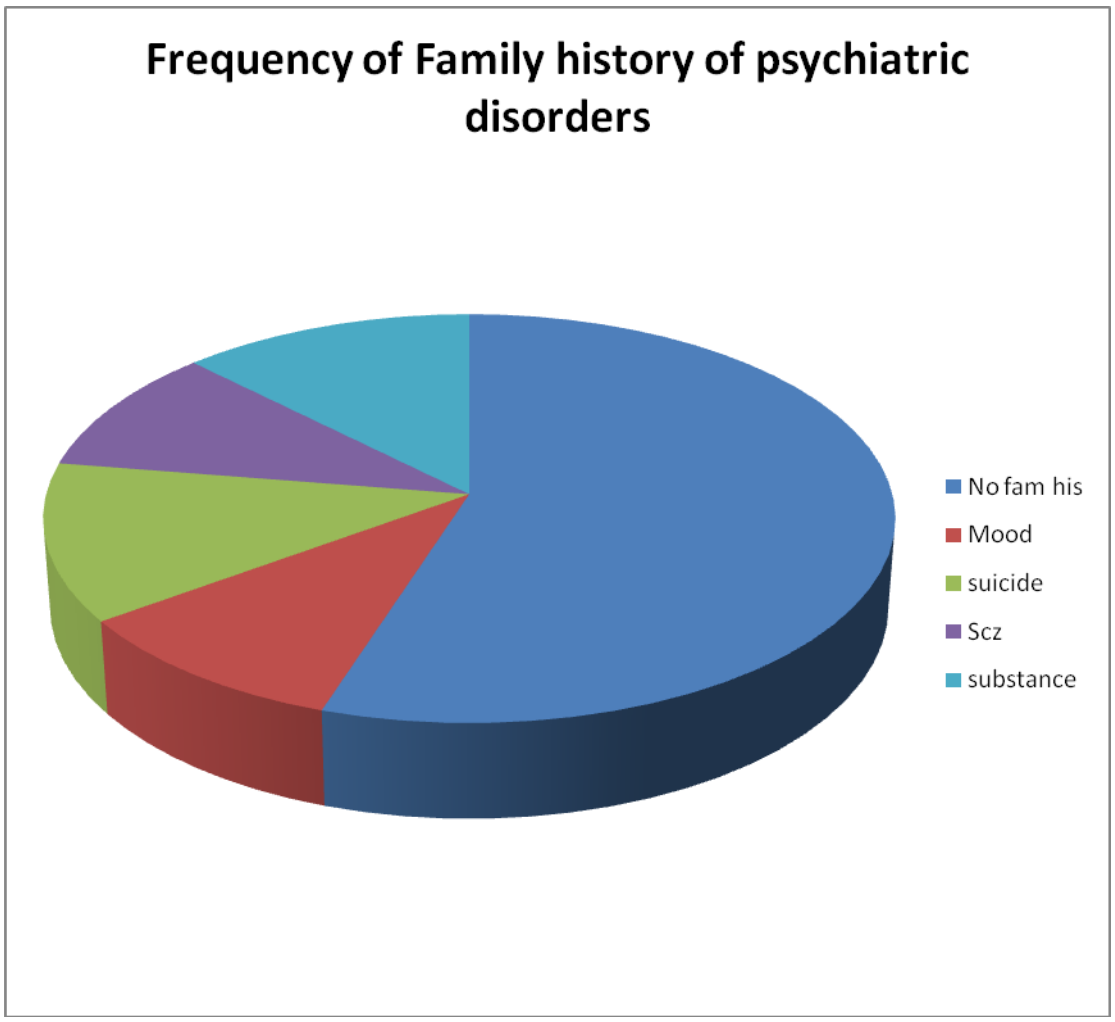
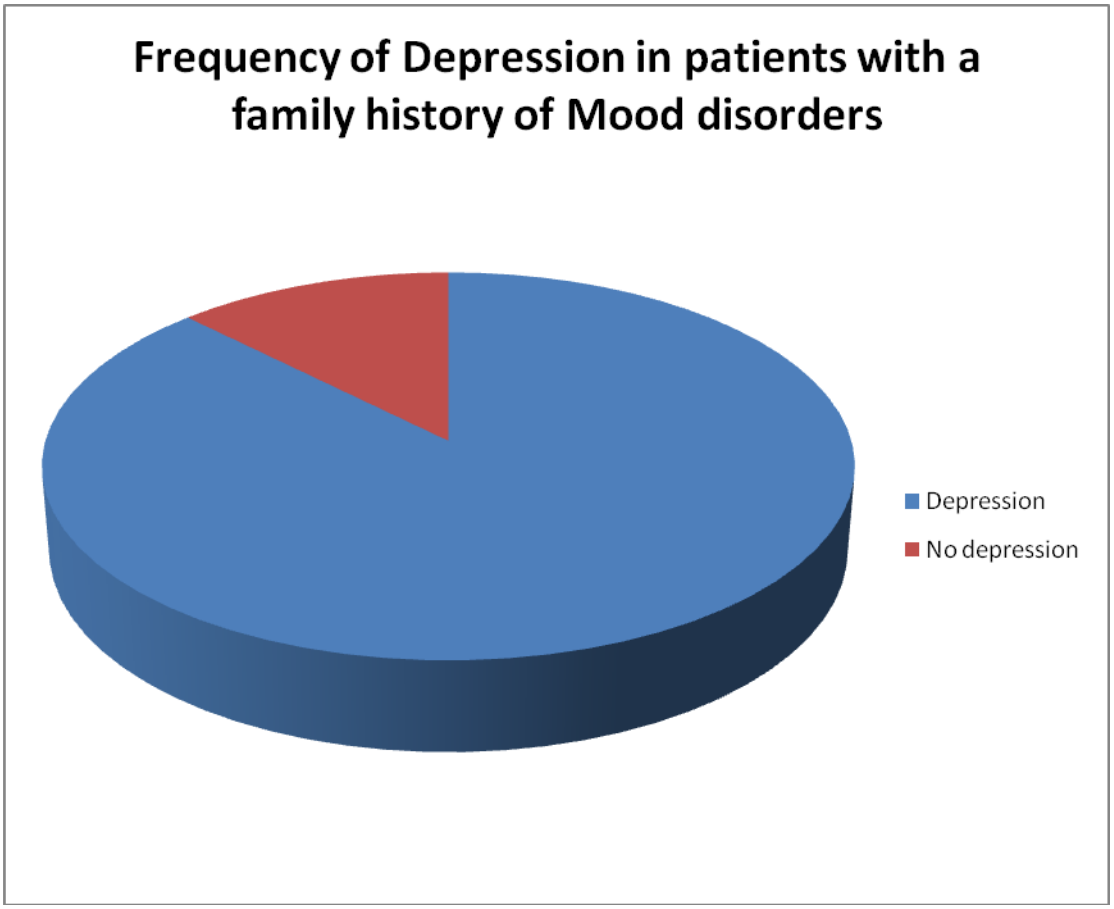

Frequency of Family history of psychiatric disorders
No fam his
Mood
suicide
Scz
substance

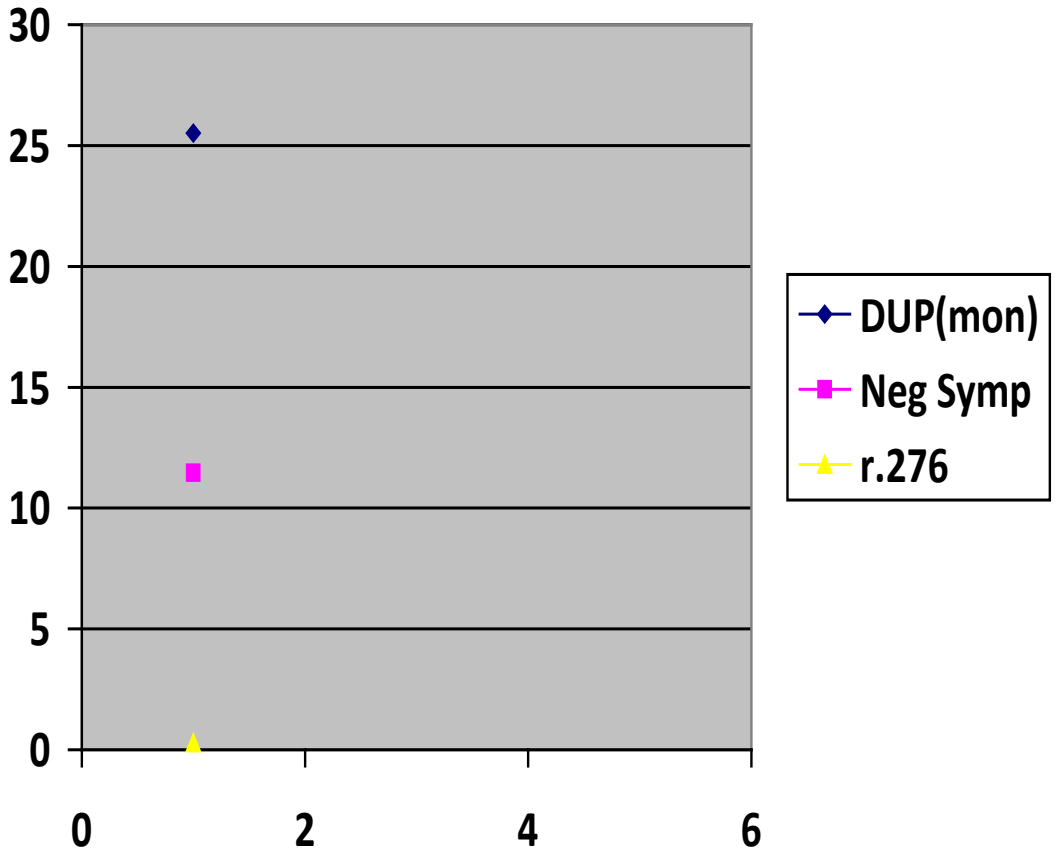
**Diagram 4**


Frequency of Depression in patients with a family history of Mood disorders
Depression
No depression

## *Scatter plots*

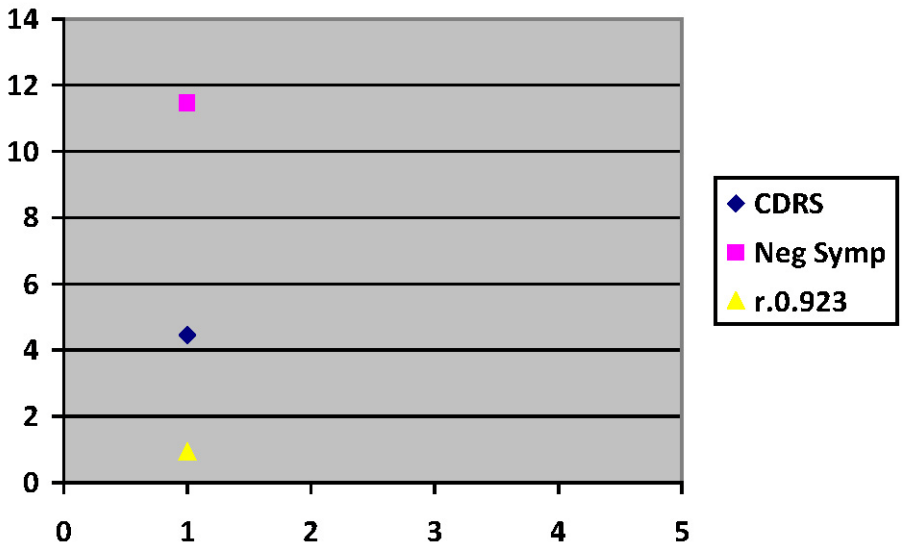
### *Relationship between mean value of Duration of Untreated Psychosis [DUP]and Negative symptoms*

### *(Scatter plot 1)*




**P-value (p. <0.05)**

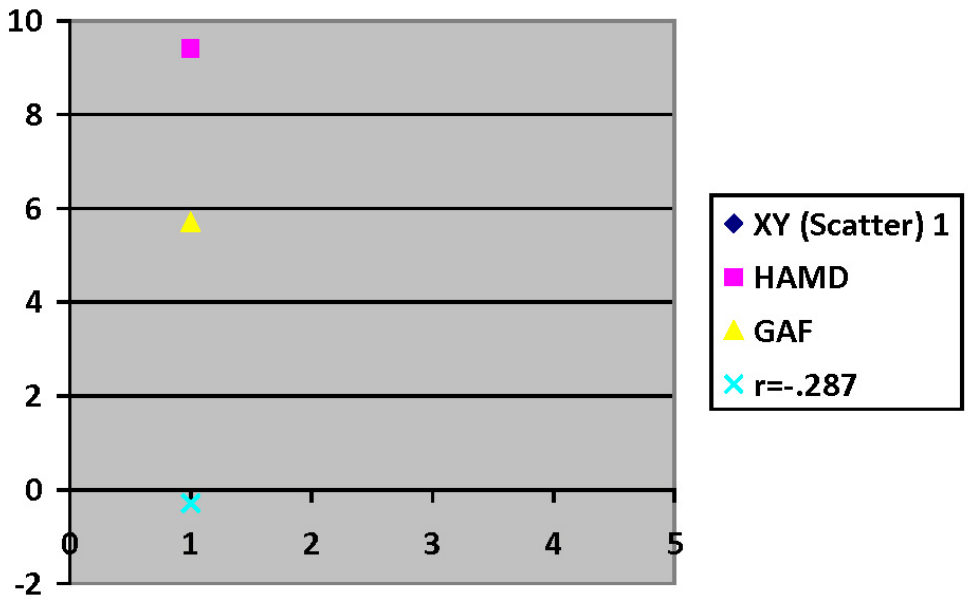
***Relationship between CDRS Score and Negative symptoms sum of PANSS (Scatterplot 2).***




**P.Value (**p. <0.01**)**

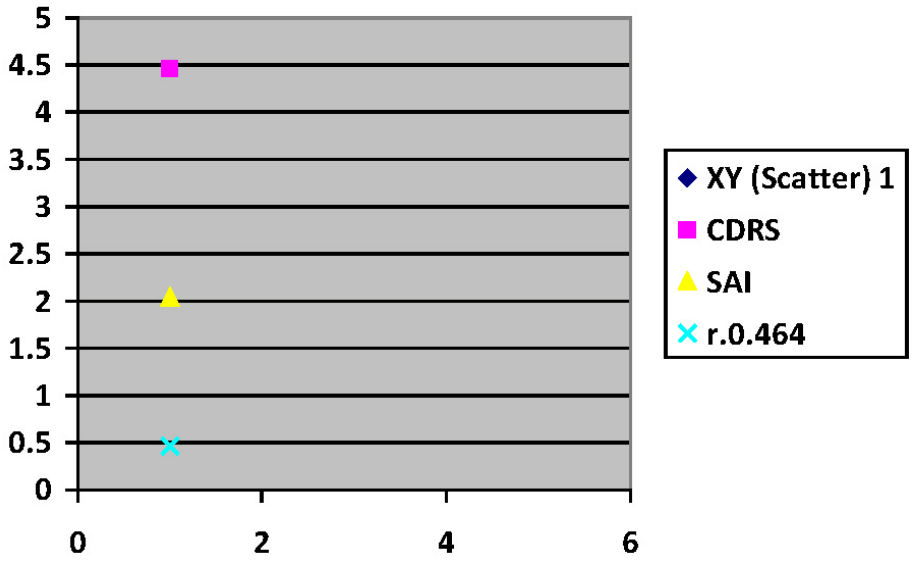
## *Relationship between HAMD score and GAF*

## *(Scatter plot 3)*




**P.Value (p<0.01)**

***Relationship between CDRS score and Schedule for Assessment of Insight (Scatter plot 4)***




**P.value(p-<0.01)**

## DISCUSSION:

This study is designed to search depression as a symptom or syndrome in persons diagnosed to be suffering from Schizophrenia. The need to segregate features of Depression from the apparently inherent constituents of Schizophrenia viz. the negative symptoms and cognitive impairments on one hand and the secondary influences caused by the disease process other than Depression and the impact of pharmacotherapy on the other hand is recognised as a challenge to clinical acumen. Any attempt to define these features is a riddle and permits much of complicating overlap. Hence instruments were chosen with care to qualitatively differentiate these features before quantifying the observations.

The scores from Calgary Depression Scale for Schizophrenia [CDSS], Hamilton Rating scale for Depression [HAM-D], and Positive and Negative Symptoms Scale [PANSS] were considered for this purpose.

80 subjects of both genders attending a tertiary care centre were consecutively taken up for the assessment.

Assessment of psychopathological dimension and the depressive symptoms were cross-sectional indicating incidence of depressive

symptoms at a point in time. Depression was measured based on rating scales of Calgary Depression scale for Schizophrenia and Hamilton depression rating scale. Assessment was done by two psychiatrists for better reliability.

In this study population 34.5% had Depressive symptoms. Some of the earlier studies rated the prevalence of depression based on the syndromal criteria and some were based on the rating scales criteria. The prevalence rate ranged from 7% to 75%. [Korean AR and Lieberman et al 1993].

The lowest rate was observed based on rating scale [Hirsch Sr and Patel M1989].The modal rate of Depression in Schizophrenia was around 25% [Maglashan TH and Carpenter WJ et al 1976].

In this investigation, 30% subjects had Major Depression[>7 points] based on the Calgary Depression scale for Schizophrenia which is the sensitive measurement separating Depression as an integral part of Schizophrenia from the secondary factors contributing for Depression in Schizophrenia. 4.5 percent of the study subjects had qualified for Minor Depression, scoring above 4 points in Calgary Depression scale for Schizophrenia. Both major and minor category was based on the CDSS score. [Addington D and Tyndale EM et al 1994].

The psychopathological aspects of the population reveals that they had a mild level of psychopathology based on the PANSS total score. This represents the stable group of subjects on antipsychotic treatment.

**Negative symptoms in schizophrenia and depression**:

The overlay of depressive symptoms with negative symptoms were variously reported in schizophrenia. [Siris SG and Casey E et al 1992]. The major differentiating symptom was mood, which distinguishes the negative syndrome profile of Schizophrenia. [Siris SG 1995]. In this study, the depressive scores on CDSS [Calgary Depression scale for Schizophrenia] and Hamilton depression rating scale had shown a statistically significant correlation with general psychopathology score of PANSS. The general psychopathology score indirectly correlates positively with negative symptoms scale of PANSS.

Based on this observation, the depressive symptoms may have an overlay of negative symptoms of Schizophrenia rather than an independent syndrome of schizophrenic illness.

Few authors have reported a positive relationship between depressive symptoms and positive symptoms of Schizophrenia. But in this study positive symptoms had negative relationship with general

psychopathology score which in turn has positive correlation with depressive scores on CDSS and HAMD.

**Depression in Schizophrenia and extra pyramidal symptoms**;

Another area of conceptual confusion has rested on extrapyramidal symptoms due to the apparent resemblance of symptoms and signs. The neurochemistry is also in close proximity. Even the pharmaco-therapeutic agents have some areas in common.

No significant correlation was found between the total scores on the extra pyramidal symptom rating scale and severity of depression by Hamilton depression rating scale or Becks depression inventory.[Herald A and Som DS et al 2008]. Akinesia and akathesia were found to have confounded in the literature. [Rifkin A and Klein DF et al 1975].

This sample did not have significant extra pyramidal symptoms on the ESRS Scale indicating that there were no drug induced neurological side effects in the study population. This may be due to the atypical antipsychotic treatment or lower therapeutic maintenance dosage of both conventional and atypical antipsychotic medications.

Depressive symptoms were present while on antipsychotic treatment. The influence of antipsychotics or the role of antipsychotic

medications cannot be commented in this sample as no pretreatment assessment is available.

Positive correlation was found between plasma levels of haloperidol and depressive symptoms. [Krakowski M and volavka J et al 19970].

**Depression in schizophrenia and Functional Outcome**:

Depressive symptoms in schizophrenia are associated with poor functioning and quality of life scores. Patients with depressive symptoms also need more number of hospitalization and are associated with a high mortality rate including suicide.

Bowie et al observed a negative correlation with functional outcome. Both depressive symptoms and negative symptoms were associated with poor functional outcome.

In this current observation, the duration of untreated Psychosis [DUP] was positively correlated with negative symptoms score of PANSS and GAF score.

This represents that delay in the initiation of treatment results in development of more negative symptoms and more functional impairment reflecting the functional outcome of the illness. Hamilton

depression rating scale score had negatively correlated with Global assessment of Functioning score.

On par with the available literature, the presence of depressive symptoms predict an unfavourable outcome of functioning.

**Depression in schizophrenia and Insight:**

The insight score was positively correlated with lower mood in many studies. Poor insight in fact protects against depression. [Ambalam P and Vadapathy P 2012].

In analogy with the previous observations, the current observation also reports that a statistically positive correlation between CDSS score, HAMD score and the scores on SAI [schedules for assessment of Insight] exists.

The degree of insight measured in three dimensions by using the SAI scale indicating direct correlation with depression rating scale scores. Schizophrenic patients are prone to develop depression when they regain their insight during the course of illness.

All the subjects in this study were having mild psychopathology in terms of rating on PANSS but their mean score on insight was very low indicating poor insight Schizophrenia group. The poor insight in the

present group may be the reason for lower degree of depressive symptoms leaving them in mild depression category.

Prevalence of Depressive symptoms in Schizophrenia is higher in patients who have a positive family history of mood disorder or suicide or alcohol dependence. It is evident from earlier studies, that a familial transmission is common in major affective disorders. Hence it seems very much reasonable to believe that the depressive symptoms appearing in patients with Schizophrenia might be the result of a familial liability for affective disorders [17]. Similar findings were evident in the researches done by Subotnik et al 1997, Kendler and Hays 1983. It is possible that this affective burden does not have a say in the psychotic process per se but instead gives it an affective colouring. It may be over simplification to conclude that Depression with genetic transmission will find its way with families where the genetic load is severe, with more number of depressed persons in its fold. It is worth recollecting at this point Slater's interpretation that depressive symptoms in relatives, particularly parents of the patient may be a phenotypic expression of the genotype schizophrenia.

Going by the stress-vulnerability model, we can arrive at the conclusion that probably the family history of affective disorders lowers the threshold for developing depressive symptoms in these patients.

**Antipsychotics and depression in Schizophrenia**

Patients on atypical antipsychotic for more than a month have low scores on CDSS scores than patients who have been on typical antipsychotic. This is in agreement with various studies conducted by Marder et al, 1997, Tollefsonn et al, 1998, Emsley et al 2003 and Mauri et al 2008 who unanimously reported that the second generation antipsychotics have been associated with reduced symptoms of Depression.

There may be various probable reasons for this superiority of atypical antipsychotics in the treatment of depressive symptoms in Schizophrenia .One way of looking at it is that, since the atypical psychotics do not exert their antipsychotic action exclusively by dopamine blockade, they rely on actions through various other receptors for their therapeutic effect and hence their chances of producing the phenomenon of neuroleptic induced dysphoria is meagre.

The atypical antipsychotics have a better side effect profile [Casey D E1997 , Tandon R 1997, Couinard G 1993, Marder S R 1994] and hence the compliance with these medications are better on the long run [Rosenheck R 1997,Song F 1997,Naber D 1998 ] thereby decreasing the incidence of Depression heralding the prodrome of a psychotic relapse.

These antipsychotics exert their action on a diverse set of receptors including dopaminergic, serotonergic, histaminergic, muscarinic and alpha 1 nor- adrenergic receptors. This diversity of actions at various receptors is probably responsible for their anti depressant action [Tollefson GD 1998, Waddington J L 1997].

Studies focussing on both Depression [Pandey G N et al 1990 ]and Schizophrenia [ Kahn R S et al 1993] have concentrated on the 5-HT2 binding site , as this can accelerate the dopamine flow across the synapse through its potential to produce presynaptic inhibition. But it would be too premature to come to a conclusion that this is the only site of action, and probably much more research is needed in this area. As of now, it is prudent to understand that the various atypical antipsychotics vary in their level of actions at various receptors and that this eventually results in a wide variation in their antidepressant efficacy. They therefore should not be assumed to be a homogeneous group.

It would be inappropriate to conclude from the effect –or lack of effect – found with one agent to apply to other atypical agents. Many molecules in this cluster have precise antidepressant activity in lower doses. In this study, the subjects received either typical or atypical antipsychotic drugs or both in moderate doses. Patients on medications,

did not have significant extrapyramidal symptoms and had a significant incidence of depression.

Based on this observation we may be justified in concluding that, the association between depression and Schizophrenia is independent of the extrapyramidal symptoms and antipsychotic medications.

Some questions arise as a result of this experience.

a. Can we consider as genetic conglomeration by chance association what we saw as depression in Schizophrenia?
b. Is depression a part and parcel of Schizophrenia?
c. Is it possible that Depression and Schizophrenia are at the two ends of a continuum?
d. Do we have to treat depression in schizophrenia with anti depressants? Will all the antidepressants be qualified for this purpose? Already some suggestion indicating benefit with Escitalopram [not Citalopram] and Fluvoxamine is available. If it is so, the widely held Dopamine theory on Depression and Schizophrenia need to go back stage, for we have to mix poison and the potion.
e. Or is it sufficient to treat Schizophrenia? Would depression in Schizophrenia clear?
f. Is it necessary to suggest even if remotely, the possibility to discard the Kraepelinean dichotomy?
g. Are we going back or forward?
h. Considering stress of Depression as a precipitator of psychosis with positive symptoms, will it be worth treating adolescent depressions more aggressively with a view to prevent a psychotic breakdown, at least in persons with high risk family history? What pharmacological strategy can be advantageous? Anti depressants or Serotonin-Dopamine receptor Antagonists?

# STRENGTHS & LIMITATIONS OF THE STUDY

## STRENGTHS:

1. Calgary Depression scale for Schizophrenia which has been found to be particularly useful in identifying and quantifying the depressive features in patients with schizophrenia has been used.
2. An adequate number of patients were included into the study to increase the statistical relevance of the study.
3. The diagnosis of schizophrenia was made by two independent observers.
4. No cut off point was used to assess the depressive symptoms. A dimensional approach was used and not the categorical approach.
5. This study had equal number of patients from rural and urban background.

## LIMITATIONS:

1. No control group was used.
2. No randomisation done in the selection of cases.

3. Patients with positive symptoms are more likely to come to the hospital and hence the sample contains more patients with positive symptoms.

4. All samples were collected from a tertiary centre and hence may not be applicable to the community.

5. We recruited patients who approached the hospital for treatment and so it is not a genuine epidemiological sample .This also increases the so –called Berkson's bias –the more conditions a patient suffers from, the higher the likelihood of seeking treatment-which leads to an over-representation of patients with multiple diagnosis in samples recruited from clinical settings .

6. No drug naive patients in the sample – to help exclude the influence of neuroleptic drugs in mimicking symptoms of depression.

7. The group was heterogeneous with respect to age, gender, duration of illness, type of Schizophrenia and the duration of treatment.

# CONCLUSION

The extent of psychiatric co-morbidity in Schizophrenia is often not appreciated; in part this is because of a heritage of an essentially hierarchial approach to psychiatric diagnosis, where Schizophrenia trumps the diagnosis of Depression. However it is essential to address the depressive symptoms in Schizophrenia as these are common, tend to worsen the longitudinal course of Schizophrenia and also results in an increase in morbidity and mortality.

The various factors that might mediate depression in Schizophrenia include

- Psychosocial stressors [ egs family stress, loss of role]
- Social factors [unemployment, lack of social network etc]
- Adjustment to diagnosis
- Adjustment to the social stigma
- Alcohol and illicit substance use
- Non compliance with antipsychotic medication
- Direct dysphoric effect of antipsychotic medication
- Extrapyramidal side effects of antipsychotic medication

Depression in Schizophrenia is reported to be associated with worse outcome, impaired functioning and personal suffering. Depression is also linked with higher rates of relapse, rehospitalisation and even suicide. This study however did not go into the therapeutic aspects.

Though Psychiatrists unanimously agree that Depression in Schizophrenia is associated with considerable clinical burden, there is no consensus regarding the best treatment strategy or a clear indication for initiating specific treatment. Thus the sensitive and specific assessment of depressive symptoms in Schizophrenia is important for diagnostic, prognostic, and therapeutic reasons.

## Future directions

I. Prospective study following adolescent Depression to determine the frequency of conversion to Schizophrenia is imminent.

II. Study of patients in the acute phase of psychosis to differentiate and elicit depressive symptoms

III. In depth study of the qualitative assessment of depressive symptoms in Schizophrenia.

IV. Therapeutic trials with addition of antidepressants and without them.

V. Study of suicide – attempt and completion and its relationship to presence of Depression or absence of it, and to determine whether suicide in Schizophrenia is more impulsive or premeditated?

VI. Treatment trials involving antidepressants to treat depression in prodrome to observe the efficacy to abort Psychotic break down.

# BIBLIOGRAPHY


1. Ian F B Rockington. A critical view of the concept of schizophrenia. In: Richard Williams and Thomas Dalby eds. Depression in schizophrenics. Plenum press p 5-13

2. Siris SG. Depression and schizophrenia. In: Schizophrenia. Hirsch SR, Weinberger DR, [eds]. Oxford, England: Blackwell science, 1998: 128-145.

3. Robins LN, Regier DA [eds]. Psychiatric disorders in America: The Epidemiologic Catchment Area Study. New York: The Free press;1991

4. Leiberman JA , Textbook of schizophrenia, American Psychiatic Publishing,2006 p227

5. Martin RL, Cloninger CR, Guze SB, Clayton PJ. Frequency and differential diagnosis of depressive syndromes in schizophrenia. J Clin Psychiatry. 1985:46 [11 Pt 2]:9-13.

6. Hafner H, Riecher-Rossler A, Hambrect M, Maurer K, Meissner S, Schmidtke A, , IRAOS; an instrument for the assessment of onset and early course of schizophrenia. Schizophrenia Res 1992 ;6[3]:209

7. Hafner H, Maurer K Loffler W an der Heiden W, Munk-Jorgensen P, Hambrecht M, ,. The ABC schizophrenia study: A preliminary overview of the results. Soc Psychiatry epidemiology 1998;33[8]:380-386

8. Bustamante S, Maurer K, Loffler W, Hafner H. Depression in early course of schizophrenia. Fortschr Neurol Psychiatry .1994;62[9]:317-329.

9. PJ Weiden: Psychological treatment of depression in schizophrenia in: Managing the depressive symptoms in schizophrenia, PE Keck Jr [editor] Panther publishers: 2000,58-73

10. Bojana Avgustin, Depression in Schizophrenia – Literature Review, Psychiatria Danubina 2009, vol 21, suppl 1, pp 93-97;

11. Siris SG. Depression in Schizophrenia: in the era of Atypical Antipsychotics, AJP 2000

12. Taylor M. Are schizophrenia and affective disorder related? A selective literature review. Am J Psychiatry 1992, 149: 22-32.

13. Crow TJ. The continuum of psychosis and its implications for the structure of the gene. Br J Psychiatry 1986,149:419-429

14. McGuffin P, Revely AM, Holland A. Identical triplets: Non identical psychosis? Br J Psychiatry 1982,140:1-6

15. Kendler and Hays 1983; Subotinik LS and Keith H, Depressive Symptoms in Early Course of schizophrenia: Relationship to familial psychiatric illness, Am J Psychiatry 1997; 154: 1551-1556**.**

16. Michael Alan Taylor, Are schizophrenia and affective disorders related? Preliminary data from a family study, Am J Psychiatry 150:2, February 1993

17. Subotnik KL, Nuechterlein KH, Asarnow RF. Depressive symptoms in the early course of schizophrenia: relationship to familial psychiatric illness. Am J Psychiatry 1997; 154:1551

18. TJ Crow. Nature of genetic contribution to psychotic illness- a continuum view point, Acta Psychiatrica Scandinavica.1990,81:401-408

19. Martin Harrow, Cynthia A.Yonan, James R Sands, Joanne Marengo, Depression in schizophrenia: Are neuroleptics, akinesia or anhedonia involved? Schizophrenia Bulletin,20[2]:327-338,1994

20. McGlashan TH: Aphanisis: the syndrome of pseudo depression in chronic schizophrenia. Schizophr Bull 1982;8:118-134

21. PF. Buckley, Brian J. Miller, Douglas S Lehrer, David J. Castle. Psychiatric comorbidities and schizophrenia, Schizophrenic Bulletin,2009,35:383-402

22. Drake RE, Cotton PG: Depression, hopelessness and suicide in chronic schizophrenia.Br J Psychiatry148:554-559,1986

23. Raju SS, Depressive disorder in schizophrenia. Indian Journal of Psychiatry1986;25:109-18

24. Bartels SJ, Drake RE. Depressive symptoms in schizophrenia: Comprehensive differential diagnosis.Compr Psychiatry.1988;29:467-483

25. SG Siris, Treating depression in patients with schizophrenia, current psychiatry, 2012, vol 11.

26. Cohen SM, Allen MG, Pollen W: Relationship of schizoaffective psychosis to manic depressive psychosis and schizophrenia. Findings in 15,909 veteran pairs. Arch Gen Psychiatry 26:539-546,1972

27. Bertelsen A: Genetic studies in schizophrenia and schizoaffective disorders, in A genetic perspective for schizophrenic and related disorders, Edited by Smeraldi E, Milan, 1988

28. SM Strakowski: The co – occurance of depression in schizophrenia In: Managing the depressive symptoms of schizophrenia, PE Keck jr[editor] Panther publisher:2000,1-9

29. D. A. W. Johnson, Depression in schizophrenia: some observations on prevalence etiology and treatment:137-142

30. Ander Heiden W , Depression in the long term course of schizophrenia, Eur Arch Psychiatry Clin Neurosci 2005;255:174-84

31. Hawton K , Schizophrenia and suicide: systematic review of risk factors, Br J Psychiatry, 2005; 187-9.

32. Glazer W, Prusoff B, John K , Depression and social adjustment among chronic schizophrenic outpatients, J Nerv Ment Dis 1981;169:712-7.

33. Kang Simbac, Rathi Mahendran , Subjective quality of life in first episode schizophrenia spectrum disorders with co-morbid depression, 2004, 129, 141-147.

34. Reine G, Lancon C, Depression and subjective quality of life in chronic phase schizophrenic patients. Acta Psychiatr Scand 2003;108:297-303

35. Gildas Brebion , Clinical correlates of memory in schizophrenia: Differential links between Depression, Positive and Negative symptoms and two types of memory impairment, Am J Psychiatry 154:11,November 1997

36. Kenji W Sax, Stephen M Strakowski, Relationships among negative, positive, and depressive symptoms in schizophrenia and psychotic depression, British Journal of Psychiatry [1996], 168,68-71

37. Paul H Lysaker, Morris D Bell, Stephen M Bioty and Wayne S Zito. The frequency of associations between positive and negative symptoms and dysphoria in schizophrenia, Comprehensive psychiatry, vol 36, no.2, 1995, pp113-117

38. R.Kulhara, A.Avasthi, R.Chadda, Negative and depressive symptoms in schizophrenia; British Journal of Psychiatry[1989]:154, 207-211.

39. Tharayan A, Kuruvilla K. The correlates of the symptom of depression in schizophrenia. Indian Journal of Psychiatry, 1994; 36:74-79.

40. Ross MG Norman and Ashok Malla; Correlations over time between dysphoric mood and symptomatology in schizophrenia; Comprehensive Psychiatry vol 35; 1994; 34-38.

41. Rathod S, Kingdon D, Smith P, and Turkington D. [2005].Insight into schizophrenia: The effects of cognitive behavioral therapy on the components of insight and association with socio demographics-Data on a previously published randomized controlled trial. Schizophr Research, 74, 211-19.

42. Carrol A. Fattah S, Clyde Z, [1999]. Correlates of insight and change in schizophrenia. Schizophr Research,35,247-53

43. Addington D, Addington J, Schissel B; A depression rating scale for Schizophrenics. Scizophr Res 1990;3:247-251

44. Collins A, Remington G, Coulter K, ,: Depression in Schizophrenia: A comparison of three measures, Schizophr Res 1996;20:205-209

45. Marder SR, Davis JM, Chouinard G. The effects of Risperidone on the five dimensions of schizophrenia derived by factor analysis: combined results of the North American trias. J Clin Psychiatry. 1997; 58[12]:538-546.

46. Tollefson GD, Sanger TM, Lu Tollefson GD, Sanger TM, Lu Y, Depressive signs and symptoms in schizophrenia: a prospective blinded trial of olanzapine and haloperidol. Arch Gen Psychiatry.1998; 55[3]:250-258.

47. Emsley RA, Buckley P, Jones AM, Differential effect of quetiapine on depressive symptoms in patients with partially responsive schizophrenia. J Psychopharmacol.2003; 17[2]:210-215.

48. Meltzer HY, Okayli G: Reduction of suicidality during clozapine treatment of neuroleptic resistant schizophrenia: Impact on risk benefit assessment. Am J Psychiatry 1995 ;152:183-190

49. Paul Plasky. Antidepressant usage in schizophrenia, schizophrenia bulletin, vol 17,no 4,1991,649-657

50. Victoria Omranifard, Ghadir Mohammad Hosseini, Mohammad Reza Sharbafchi, Mohammad Maracy, Fatemeh Ghasemi, Mahin Aminoroaia. Sertraline as an add-on treatment for depressive Symptoms in stable schizophrenia:A double-blind randomized controlled trial. Journal of Research in Medical Sciences, March 2012 Special Issue

51. Thomson Healthcare Inc. 2000 Physicians'desk reference.Montvale [NJ]: Thomson Healthcare Inc. 1999.

52. A.R.Koreen, MD, SG Siris, Miranda Chakos, Jose Avir, David Mayerhoff, Jeffrey Lieberman. Depression in first episode schizophrenia.Am J Psychiatry150:11; 19931643-48.

53. Douglas F Levinson , Treatment of schizoaffective disorder and Schizophrenia with mood symptoms; Am J Psychiatry 156:8, August 1999

54. K.Felmet, S.zisook, W. Kasckow ;Elderly patients with schizophrenia and depression: Diagnosis and treatment: clinical schizophrenia and related psychoses an 2011;239-250

55. Samuel G Siris, Treating depression in patients with schizophrenia; Current Psychiatry: sept-oct 2012;20-25

56. Massimo C. Mauri, Depression in Schizophrenia: Comparison of first- and second- generation antipsychotic drugs. Schizophr Research, vol 99. Issue 1,pp 7-12,Feb 2008

57. Hawton K, Sutton L, Haw C, Schizophrenia and suicide: Systematic review of risk factors. Br J Psychiatry.2005;187:9-20

58. Baynes D, Depressive symptoms in stable chronic schizophrenia; Prevalence and relationship to psychopathology and treatment. Schizophr Res, 2000 Sept 29;45[1-2]:47-56

59. D. D. Addington, Clinical issues related to depression in schizophrenia: an International survey of psychiatrists, Acta psychiatric Scandinavia, vol.105, 2002, 189-195.

60. David Castle and Til Wykes, Depression and Anxiety in Schizophrenia In: Pharmacological and psychosocial treatments in Schizophrenia edited by David Castle , 2003,Matrin Dunitz Ltd, pg 63-75

# APPENDIX

## APPENDIX - I

## SOCIO DEMOGRAPHIC DATA SHEET

Serial No: ____ OP. No: _____

Name: _____ Age: Sex:

Marital status: Unmarried Married Separated

Religion: Hindu Christian Muslim Other

Education in Years: _____ Employment: Yes No

Nature of Work: Manual Unskilled Skilled

Income Class: <900 900 - 3000 3001 - 9999 > 10,000

Residence: Urban Rural

## CLINICAL DATA SHEET

Type of Schizophrenia: Paranoid Undifferentiated Catatonic

Residual Disorganized Other

First Episode: Yes No Age at Onset: _____

Duration Untreated: _____ Age at First Hospitalisation: _____

Number of Admissions: ___ Duration of Illness :< 2 yrs, 2-5yrs, >5 yrs in months

____

Family History: Yes No

Mood disorder

Suicide

Alcohol Dependence

Handedness: Right Left

Current Treatment: Typicals Atypicals

Last Prescription:

H/o treatment with antidepressants:
H/o treatment with Lithium:
Current Substance Use: Yes No
Medical illness:

## APPENDIX - II

# POSITIVE AND NEGATIVE SYNDROME SCALE

| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|---|
| **POSITIVE SYMPTOMS** | | | | | | | | |
| P1 | DELUSIONS | | | | | | | |
| P2 | CONCEPTUAL DISORGANISATION | | | | | | | |
| P3 | HALLUCINATORY BEHAVIOUR | | | | | | | |
| P4 | EXCITEMENT | | | | | | | |
| P5 | GRANDIOSITY | | | | | | | |
| P6 | SUSPICIOUSNESS | | | | | | | |
| P7 | HOSTILITY | | | | | | | |
| **NEGATIVE SYMPTOMS** | | | | | | | | |
| N1 | BLUNTED AFFECT | | | | | | | |
| N2 | EMOTIONAL WITHDRAWAL | | | | | | | |
| N3 | POOR RAPPORT | | | | | | | |
| N4 | PASSIVE /APATHETIC SOCIAL WITHDRAWAL | | | | | | | |
| N5 | DIFFICULTY IN ABSTRACT THINKING | | | | | | | |
| N6 | LACK OF SPONTAENITY AND FLOW OF CONVERSATION | | | | | | | |
| N7 | STEREOTYPED THINKING | | | | | | | |
| **GENERAL PSYCHOPATHOLOGY SYMPTOMS** | | | | | | | | |
| GI | SOMATIC CONCERN | | | | | | | |
| G2 | ANXIETY | | | | | | | |
| G3 | GUILT FEELING | | | | | | | |
| G4 | TENSION | | | | | | | |
| G5 | MANNERISMS/POSTURING | | | | | | | |
| G6 | DEPRESSION | | | | | | | |
| G7 | MOTOR RETARDATION | | | | | | | |
| G8 | UNCOOPERATIVENESS | | | | | | | |
| G9 | UNUSUAL THOUGHT CONTENT | | | | | | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| G10 | DISORIENTATION | | | | | | | |
| G11 | POOR ATTENTION | | | | | | | |
| G12 | LACK OF INSIGHT AND JUDGEMENT | | | | | | | |
| G13 | DISTURBANCE OF VOLITION | | | | | | | |
| G14 | POOR IMPULSE CONTROL | | | | | | | |
| G15 | PREOCCUPATION | | | | | | | |
| G16 | ACTIVE SOCIAL AVOIDANCE | | | | | | | |

**PANSS PROFILE SUMMARY**

| | RAW TOTAL | PRECENTILE | RANGE |
|---|---|---|---|
| SCALES | | | |
| POSITIVE SYNDROME [sum of P1 to P7] | | | |
| NEGATIVE SYNDROME [sum of N1 to N7] | | | |
| COMPOSITE INDEX [PS – NS ] | | | |
| GENERAL PSYCHOPATHOLOGY [sum of G1 to G 16] | | | |

**CLUSTER SCORES**

| | |
|---|---|
| ANERGIA | N1 + N2 + G7 + G10 |
| THOUGHT DISTURBANCE | P2 + P3 + P5 + G9 |
| ACTIVATION | P4 + G4 + G5 |
| PARANOID / BELLIGERANCE | P6 + P7 + G8 |
| DEPRESSION | G1 + G2 + G3 + G6 |

## APPENDIX - III

## THE CALGARY DEPRESSION SCALE FOR SCHIZOPHRENIA [CDSS]

| | | 0 | 1 | 2 | 3 |
|---|---|---|---|---|---|
| 1 | Depression | | | | |
| 2 | Hopelessness | | | | |
| 3 | Self depreciation | | | | |
| 4 | Guilty ideas of reference | | | | |
| 5 | Pathological guilt | | | | |
| 6 | Morning depression | | | | |
| 7 | Early wakening | | | | |
| 8 | Suicide | | | | |
| 9 | Observed depression | | | | |

## APPENDIX - IV

# HAMILTON DEPRESSION RATING SCALE

| S.NO | **ITEMS** | 0 | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|---|
| 1 | DEPRESSED MOOD | | | | | |
| 2 | FEELING OF GUILT | | | | | |
| 3 | SUICIDE | | | | | |
| 4 | INSOMNIA[ EARLY] | | | | | |
| 5 | INSOMNIA [MIDDLE] | | | | | |
| 6 | INSOMNIA [LATE] | | | | | |
| 7 | WORK AND ACTIVITIES | | | | | - |
| 8 | RETARDATION | | | | | |
| 9 | AGITATION | | | | | |
| 10 | ANXIETY [PSYCHIC] | | | | | |
| 11 | ANXIETY [ SOMATIC] | | | | | |
| 12 | SOMATIC SYMPTOMS-GI | | | | | |
| 13 | SOMATIC SYMPTOMS-GENERAL | | | | | |
| 14 | GENITAL SYMPTOMS | | | | | |
| 15 | HYPOCHONDRIASIS | | | | | - |
| 16 | LOSS OF WEIGHT | | | | | - |
| 17 | INSIGHT | | | | | |

# APPENDIX - V

## GLOBAL ASSESSMENT OF FUNCTIONING [GAF] SCALE

**100-91**: Superior functioning .No symptoms.

**90-81**: Absent or minimal symptoms, no more than everyday problems or concerns

**80-71**: symptoms are they are transient and expectable reactions to psychosocial stressors, mild social dysfunction

**70-61**: Some mild symptoms OR some difficulty in social, occupational, or school functioning, but generally functioning pretty well.

**60-51:** Moderate symptoms OR moderate difficulty in social, occupational, or school functioning.

**50-41**: Serious symptoms OR any serious impairment in social, occupational functioning

**40-31**: Some impairment in reality testing or communication OR major impairment in several areas such as work or school, family relations, judgment, thinking, or mood

**30-21**: Behavior is considerably influenced by delusions or hallucinations OR serious impairment in communication or judgment OR inability to function in almost all areas.

**20-1:** Some danger of hurting self or other OR occasionally fails to maintain minimal personal hygiene OR gross impairment in communication.

**10-1:** Persistent danger of severely hurting self or others OR persistent inability to maintain minimal personal hygiene OR serious suicidal act with clear expectation of death.

**0**: Inadequate information.

## APPENDIX - VI

## SCHEDULE FOR ASSESSMENT OF INSIGHT

1a. Does patient accept treatment?

1b. Does patient ask for treatment unprompted?

2a. Ask patient “Do you think you have illness?” or “Do you think there is something wrong with you?”

2b. Ask the patient “Do you think you have mental/psychiatric illness?”

2c.Ask patient “How do you explain your illness?”

3a. Ask patient “do you think the belief that [insert specific delusion] is not really true/happening? Or “Do you think that... [insert specific hallucination] is not really there / happening?”

3b. Ask patient “How do you explain these phenomena [the belief that hearing that voice /seeing that image, etc]?”

| | 0 | 1 | 2 |
|---|---|---|---|
| 1a | | | |
| 1b | | | |
| 2a | | | |
| 2b | | | |
| 2c | | | |
| 3a | | | |
| 3b | | | |

Total score =

## APPENDIX - VII

## EXTRAPYRAMIDAL SYMPTOM RATING SCALE

### I.PARKINSONISM, DYSTONIA AND DYSKINESIA:QUESTIONAIRRE

| | | 0 | 1 | 2 | 3 |
|---|---|---|---|---|---|
| **1** | Impression of slowness or weakness: difficulty in carrying out routine tasks. | | | | |
| **2** | Difficulty walking or with balance | | | | |
| **3** | Difficulty swallowing or with talking | | | | |
| **4** | Stiffness, stiff posture | | | | |
| **5** | Cramps or pains in limbs, back or neck | | | | |
| **6** | Restless,nervous,unable to stand still | | | | |
| **7** | Tremors,shaking | | | | |
| **8** | Oculogyric crisis or abnormal sustained posture | | | | |
| **9** | Increased salivation | | | | |
| **10** | Abnormal involuntary movements of extremities or trunk | | | | |
| **11** | Abnormal involuntary movements of tongue,jaw,lips or face | | | | |
| **12** | Dizziness when standing up | | | | |

### II. PARKINSONISM : EXAMINATION

| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|---|
| 1 | Expressive automatic movements | | | | | | | |
| 2 | Bradykinesia | | | | | | | |
| 3 | Rigidity | | | | | | | |
| 4 | Gait & posture | | | | | | | |
| 5 | Tremor | | | | | | | |
| 6 | Akathesia | | | | | | | |
| 7 | Sialorrhea | | | | | | | |
| 8 | Postural instability | | | | | | | |

## III. DYSTONIA : EXAMINATION

## ACUTE TORSION DYSTONIA

| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|---|
| 1 | Right upper limb | | | | | | | |
| 2 | Left upper limb | | | | | | | |
| 3 | Right lower limb | | | | | | | |
| 4 | Left lower limb | | | | | | | |
| 5 | Head | | | | | | | |
| 6 | Jaw | | | | | | | |
| 7 | Tongue | | | | | | | |
| 8 | Lips | | | | | | | |
| 9 | Eyes | | | | | | | |
| 10 | Trunk | | | | | | | |
| 11 | Other | | | | | | | |

**TOTAL = ____**

**NON ACUTE OR CHRONIC**

| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|---|
| 1 | Right upper limb | | | | | | | |
| 2 | Left upper limb | | | | | | | |
| 3 | Right lower limb | | | | | | | |
| 4 | Left lower limb | | | | | | | |
| 5 | Head | | | | | | | |
| 6 | Jaw | | | | | | | |
| 7 | Tongue | | | | | | | |
| 8 | Lips | | | | | | | |
| 9 | Eyes | | | | | | | |
| 10 | Trunk | | | | | | | |
| 11 | Other | | | | | | | |

**TOTAL = ____**

## IV. DYSKINETIC MOVEMENTS : EXAMINATION

| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|---|
| 1 | Lingual movements | | | | | | | |
| 2 | Jaw movements | | | | | | | |
| 3 | Bucco-labial movements | | | | | | | |
| 4 | Truncal movements | | | | | | | |
| 5 | Upper extremities | | | | | | | |
| 6 | Lower extremities | | | | | | | |
| 7 | Other involuntary movements | | | | | | | |

## GLOBAL ITEMS

V. Clinical global impression of severity of Parkinsonism ____

VI .Clinical global impression of severity of Dystonia ____

VII.Clinical global impression of severity of Dyskinesia ____

VIII.Clinical global impression of severity of Akathesia ____

## STAGE OF PARKINSONISM

IX. Stage of parkinsonism ____

# APPENDIX - VII

# INFORMATION SHEET

- You have been accepted into the study.
- We are conducting a study on Frequency and Characterization of Depressive symptoms in Schizophrenia in patients attending Institute of Mental Health, Chennai and for that your Participation may be valuable to us.
- The purpose of this study is to identify the frequency and characterisation of depressive symptoms in Patients with Schizophrenia.
- We are selecting certain cases and if you are found eligible, we may be getting certain details from you which will not affect your final report or management.
- The privacy of the patients in the research will be maintained throughout the study.
- In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.
- Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your

decision will not result in any loss of benefits to which you are otherwise entitled.

- The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of investigator Signature of participant

Date:

# INFORMED CONSENT FORM

**Title of the study: "Frequency and Characterization of Depressive symptoms in Schizophrenia".**

**Name of the Participant:**

**Name of the Principal [Co-Investigator]:**

**Name of the Institution: Institute of Mental Health,Chennai**

**Documentation of the informed consent**

I _____ have read the information in this form [or it has been read to me].

I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent to be included as a participant in "Frequency and Characterization of Depressive symptoms in Schizophrenia".

1. I have read and understood this consent form and the information provided to me.

2 I have had the consent document explained to me.

3. I have been explained about the nature of the study.

4. I have been explained about my rights and responsibilities by the investigator.

5. I have been informed the investigator of all the treatments I am taking or have taken in the past_____ months including any native [alternative] treatment.

11. I am also aware that the investigator may terminate my participation in the study at any time, for any reason, without my consent. *****

12. I hereby give permission to the investigators to release the information obtained from me as a result of participation in this study to the regulatory authorities, Govt. agencies, and IEC. I understand that they are publicly presented.

13. I have understood that my identity will be kept confidential if my data are publicly presented

14. I have had my questions answered to my satisfaction.

15. I have decided to be in the research study.

I am aware that if I have any question during this study, I should contact the investigator. By signing this consent form I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

**For adult participants:**

Name and signature / thumb impression of the participant [or legal representative if participant incompetent]

Name _____ Signature_____

Date_____

Name and Signature of impartial witness [required for illiterate patients]:

Name _____ Signature_____

Date_____

Address and contact number of the impartial witness:

Name and Signature of the investigator or his representative obtaining consent:

Name _____ Signature_____

Date_____

# ஆராய்ச்சி தகவல் தாள்

ஆய்வாளர் :

பங்கேற்பாளர் பெயர் :

தலைப்பு : **மனசிதைவு நோயின் மனசோர்வின் அறிகுறிகள் தென்படுதலும் அதன் தன்மையும்.**

ஆராய்ச்சியின் நோக்கம் :

மனசிதைவு நோயாளிகளிடம் மனசோர்வு நோய் அதிகமாக காணப்படுகிறது. இந்நோயின் தனித்தன்மையை கண்டறிவதே இந்த ஆய்வின் நோக்கமாகும்.

தாங்கள் இந்த மருத்துவ ஆய்வில் கலந்து கொள்ளுமாறு அழைக்கிறோம். இந்த ஆய்வானது எந்தவொரு மருத்துவ தலையீடும் இல்லாதது.

இதில் உங்களுக்கு எந்தவொரு ஆதாயமோ அல்லது ஆபத்தோ இருக்காது.

எங்கள் மையத்தில் நடைபெற இருக்கும் ஓர் ஆராய்ச்சிக்கு உங்கள் ஒத்துழைப்பும், ஒப்புதலையும் வேண்டுகிறோம்.

முடிவுகளை அல்லது கருத்தகளை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின்போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

இந்த சிறப்புப் பரிசோதனைகளின் முடிவுகளை ஆய்வின் முடிவின்போது தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

# ஒப்புதல் படிவம்

_____என்பவரின் மகனாகிய_____

என்னும் நான் “ மனசிதைவு நோயின் மனசோர்வின் அறிகுறிகள் தென்படுதலும் அதன் தன்மையும்” பற்றிய தன்னார்வருக்கான தகவல் தாளை படித்துள்ளேன். இந்த ஆய்வில் பங்குபெற நான் தகுதி உள்ளவர் என்று ஆய்வாளர்கள் முடிவெடுத்தால், நான் ஆய்வில் பங்கு பெருவேன். மேலும் ஆராய்ச்சி நிபுணர்களுடன் இந்த ஆய்வின் நோக்கம், இதன் வழிமுறைகள் எதிர்நோக்கும் பயங்கள், பாதுகாப்பு வழிமுறைகள், ஆய்வு பாடங்களை குறித்தும், உரிமைகளைக் பாதுகாப்பது குறித்தும் கலந்துரையாடியுள்ளேன். எனக்கு எழும் கேள்விகளைக் கேட்டு அவற்றிற்கு திருப்திகரமான பதில்கள் அளிக்கப்பட்டது, எழுத்து மூலமாகவும் பதில்கள் அளிக்கப்படும் என்பதை புரிந்து கொண்டுள்ளேன்.

எனது விருப்பத்தின் பேரிலேயே நான் இந்த ஆய்வில் பங்கேற்கிறேன். என்னால் இதில் பங்கேற்காமல் விலகிக் கொள்ளவும் செய்யலாம் என்பதை புரிந்து கொண்டுள்ளேன். மேலும் எந்த ஒரு காரணத்திற்காகவும், இந்த ஆய்விலிருந்து என்னால் நான் விருப்பப்பட்டால் விலகிக் கொள்ள முடியும் என்பதையும் அறிந்துள்ளேன்.

இந்த ஆய்வில் நான் ஒரு ஆய்வு செய்யப்படும் நபராக இருந்தால் எனது உரிமைகள் குறித்து ஏதேனும் கேள்விகள் எழும்பினால். நான் ஆராய்ச்சியாளர்களை எந்த நேரமும் தொடர்பு கொண்டு சந்தேகங்களை நிவர்த்தி செய்து கொள்வேன்.

மேலும் இந்த ஆய்வில் ஒரு பங்கேற்பாளர் என்ற முறையில் சட்டத்திற்கு தேவைப்படும் சந்தர்ப்பங்களைத் தவிர பிற சமயங்களில் இந்த ஆய்வுத் தொடர்பான எனது அடையாளம் மருத்துவ ஆவணங்கள் மற்றும் தகவல்கள் ரகசியமாக வைக்கப்பட்டிருக்கும் என்பதை நான் அறிந்துகொண்டுள்ளேன்.

இந்த ஆய்வு மற்றும் இதிலுள்ள பயன்கள் குறித்து அனைத்து தகவல்களையும் நான் முழுமையாக அறிந்துகொண்டு, அதன்படி ஆய்வு வழிமுறைகளை மேற்கொள்ள நான் ஒப்புதல் அளிக்கிறேன். இந்த ஒப்புதல்படிவத்தில் நகல் ஒன்றினை நான் பெற்றுக்கொண்டேன்.

பங்கேற்பாளர் பெயர் :

கையொப்பம் :

நாள் :

முதன்மை ஆய்வாளர் :

கையொப்பம் :

நாள் :

**INSTITUTIONAL ETHICS COMMITTEE**
**MADRAS MEDICAL COLLEGE, CHENNAI -3**

Telephone No: 04425305301
Fax : 04425363970

## CERTIFICATE OF APPROVAL

To
Dr. Mridula Pradeep
PG in MD Psychiatry
Madras Medical College, Chennai -3.

Dear Dr. Mridula Pradeep

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the proposal entitled "Frequency and characterization of Depression in Schizophrenia " No. 12082011.

The following members of Ethics Committee were present in the meeting held on 16.08.2011 conducted at Madras Medical College, Chennai -3.

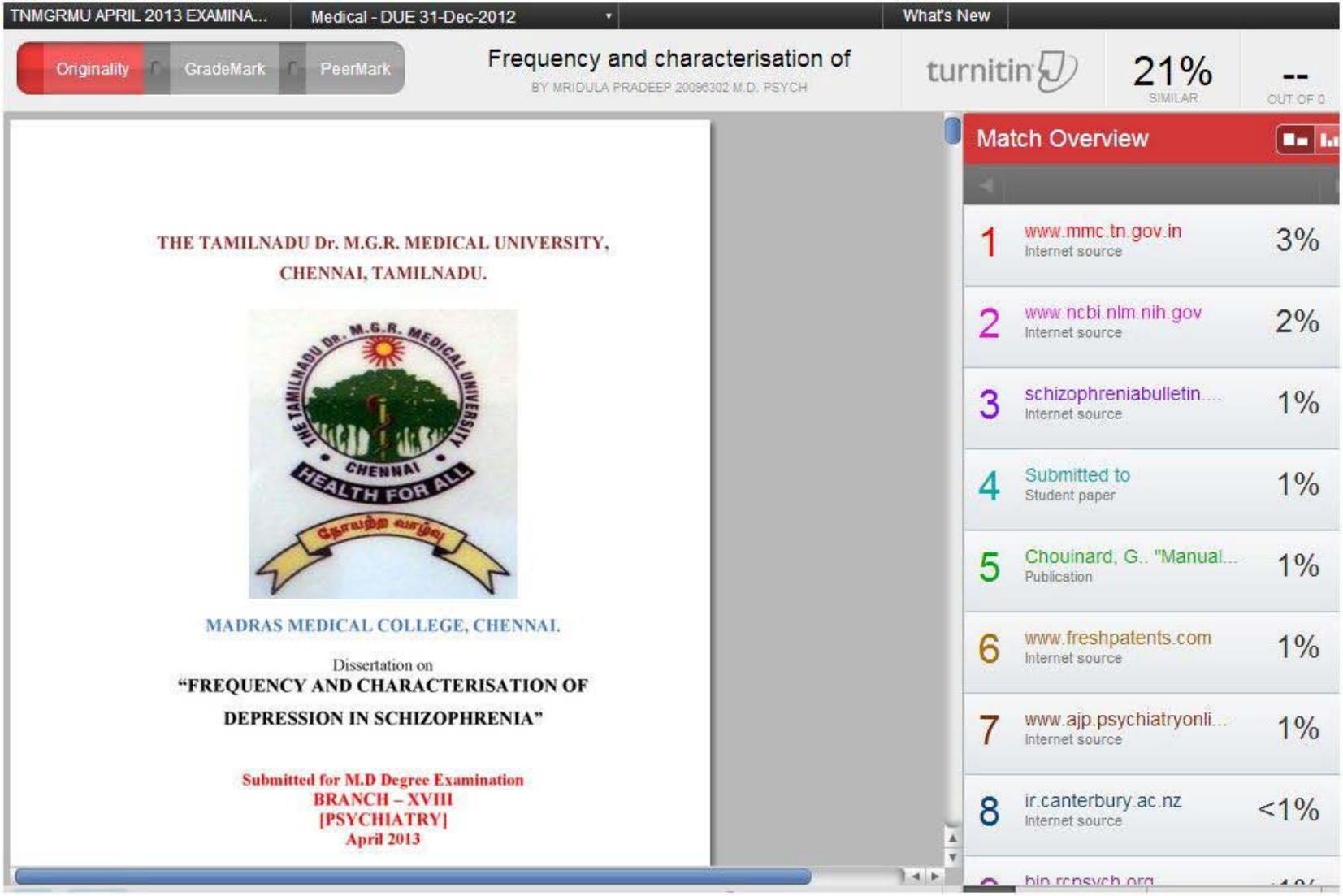
| | | |
|---|---|---|
| 1. | Prof. S.K. Rajan, MD | -- Chairperson |
| 2. | Prof. V. Kanagasabai, MD<br>Dean, Madras Medical College, Chennai-3, | -- Deputy Chairman |
| 3. | Prof. A. Sundaram, MD<br>Vice Principal , Madras Medical College, Chennai -3 | -- Member Secretary |
| 4. | Prof R. Sathianathan , MD | -- Member |
| 5. | Prof R. Nandhini, MD<br>Director, Institute of Pharmacology, MMC, Ch-3 | -- Member |
| 6. | Prof. C. Rajendiran, MD<br>Director , Institute of Internal Medicine, MMC, Ch-3 | -- Member |
| 7. | Thiru. A. Ulaganathan<br>Administrative Officer, MMC, Chennai -3 | -- Layperson |
| 8. | Thiru. S. Govindasamy . BA.BL | -- Lawyer |
| 9. | Tmt. Arnold Soulina MA | -- Social Scientist |

We approve the proposal to be conducted in its presented form

Sd /. Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report

Member Secretary, Ethics Committee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